Research Highlights 2010

IOWA STATE UNIVERSITY

Department of Mathematics

Graduate student Jyy-I (Joy) Hong works on branching processes research with distinguished professor Krishna Athreya.

Cover fractal created by Dan Ashlock.

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It is my pleasure to present the first research brochure of the Department of Mathematics at Iowa State University, *Research Highlights 2010*. This brochure highlights some of the research performed by 12 of our faculty members, a selection that is somewhat random in nature and other research profiles will follow in the coming years. To provide the reader with an overview of departmental research activity, we are including research publications of 2009/10 for (almost) all members of the faculty.

This is the first departmental publication devoted to research: Neither *mathematics news* (published until 1992) nor *Math Matters* (published since 2007) provided sufficient space to emphasize research accomplishments. We plan to make *Research Highlights* a biennial event and distribute it to supporters and stakeholders of the department, mainly in electronic form.

Many of you, and many of us in the Department, doubt that it is possible to give some impression of mathematical research in a form that is accessible to anybody with a broad science/liberal arts education. I hope this brochure proves the opposite: interesting individual articles that show at least some of the old and new mathematics that makes things work. We have avoided any technical details, but included actual and potential applications to show the breadth of topics faculty in the Department are seriously thinking about. If you are interested in more specific information about any of the articles, please contact the corresponding researcher.

As in other sciences, the quality of mathematical research and of the associated graduate programs strongly influence each other. During the last few years, the 'Mathematics' and 'Applied Mathematics' graduate programs have made tremendous progress: We now have over 80 graduate students, 74 of these are in the PhD program, including 23 female and 9 ethnic minority students. Over the last three years, we have graduated (on the average) 8 PhD and 6 MS students. And, as the list of research publications at the end of this brochure shows, our PhD students are quite active in publishing.

Members of the Discrete Mathematics Research Cluster talk after a seminar.

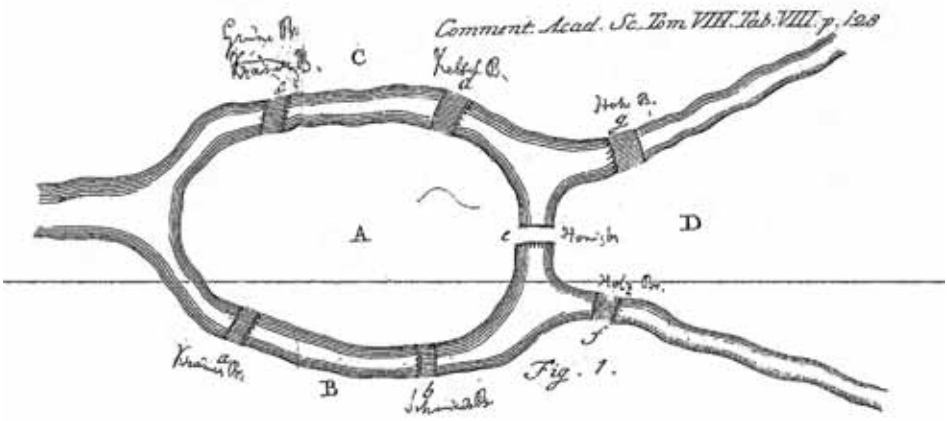
Of course, the Department has also increased its instructional responsibilities over the last years: We now teach more student credit hours than ever before (more than any other department on campus), and for the last two years we have seen record numbers of incoming students declaring 'mathematics' as their major. We have created a Center for Excellence in Undergraduate Mathematics Education with Elgin Johnston as director. This Center helps us maintain the balance between our instructional and research missions, not an easy task when both areas show important and promising growth.

If you enjoyed reading the articles in this brochure, or if you have comments or remarks, we would like to hear from you. You may email me at *kliemann@iastate.edu*, or send mail to the Department of Mathematics, 396 Carver Hall, Iowa State University, Ames IA 50011.

Wolfgang Kliemann
Professor and Chair

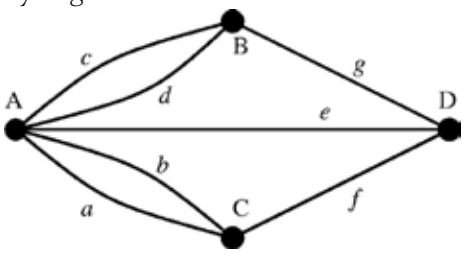
From bridges to graph theory

Before it was known as Kaliningrad, the Russian city on the Baltic Sea was once the Prussian village of Königsberg and the source of a famous mathematical puzzle. The Pregel river divided the city into 4 land masses spanned by 7 bridges. A question asked by the locals is whether a traveler could traverse each bridge exactly once and return home. Legendary mathematician Leonhard Euler, by abstracting the problem and treating it as pure mathematics, proved that this could not be accomplished by that particular arrangement of bridges.



Euler's original diagram of the bridges of Königsberg

It is difficult to imagine that Euler had envisaged that this small brainteaser, the origin of what is now known as "graph theory," would be an essential tool in answering questions of microchip design, the structure of the internet, computer science or information theory. Graphs, sometimes called networks, are an inextricable part of modern science, that were first developed as pure mathematical structures. Graphs are easily visualized as points connected by edges.



The graph corresponding to Euler's diagram. The points (or, vertices) A,B,C,D correspond to the 4 landmasses and the edges *a,b,c,d,e,f,g* correspond to the 7 bridges.

The history of graph theory is replete with incidents of unintended discoveries. In 1930, Frank Ramsey answered an important question in symbolic logic. Embedded in the proof, however, was an unexpected result on graphs. Roughly speaking, it says that in any network – no matter how complicated – there is a relatively large, "ideal", subgraph such that either every two of its points are connected by an edge, or every two of its points have no edge between them. I.e., an "ideal" subgraph is either a clique or co-clique. In the words of Theodore Motzkin, Ramsey's theorem states that "complete disorder is impossible."

The network aspect of Ramsey's result received so little attention that it was rediscovered by Paul Erdős and George Szekeres in 1935. It was Erdős who coined the term "Ramsey theory," naming it for the Scottish logician.

Finding how large this ideal subgraph must be is a fundamental question, but one that didn't concern Ramsey. In 1959, Paul Erdős and Alfred Rényi made an attempt to gain better understanding of Ramsey theory. In order to do so, they invented the first notion of a random graph. In their model, deciding whether two points are connected by an edge is random (and independent), like the flipping of a coin for each pair of points. This random graph model now inundates computer science, physics and related fields. Even though more complex and sophisticated models have since been developed, the Erdős- Rényi model is still the best for many applications. Yet, for the two Hungarian mathematicians, their interest was motivated solely by theory.

The boundary between abstract theory and concrete applications is consistently blurred in graph theory and in the more general field of discrete mathematics. In 2003, Maria Axenovich and Ryan Martin of the Department of Mathematics at ISU, together with Louisville professor André Kézdy, investigated a problem motivated by evolutionary biology. This research turned out to be yet another example of unexpected discovery.

The question was asked by a group that included ISU computer science professors Oliver Eulenstein and David Fernández-Baca who wanted to know how many changes are sufficient to perform on one evolutionary tree to make it compatible with another evolutionary tree, or how many obstructions make two evolutionary trees incompatible. The mathematicians, however, were interested in a more general question: "How much work is required to eliminate any fixed undesired

substructure in a combinatorial structure?"

Axenovich and Martin called the problem "the edit distance problem." It is related not only to biology but also to an important subfield of computer science known as property testing, which is devoted to finding efficient algorithms that decide whether a given network does or does not exhibit certain behavior.

The methods used to prove theorems in the edit distance problem relate to some of the most profound and fundamental results in the theory of graphs, such as Szemerédi's regularity lemma. This lemma links, again quite surprisingly, graph and number theory. There was a lot of excitement in the air when, in the 70's, the news broke about Endre Szemerédi proving that among any positive proportion of integers, there is always an arbitrarily long arithmetic progression. For example, if one picks, arbitrarily, 0.1 percent of the first 3 billion integers, the chosen set will contain a sufficiently long progression like 3, 14, 25, 36, 47, 58.... Szemerédi's lemma, the main tool in proving this very deep number theoretic result is, in fact, a theorem describing the regular behavior of graphs.

In general, professors Axenovich and Martin are most interested in what one can conclude about a large, complicated graph by only knowing general properties of small subgraphs. This subject – which contains the edit distance problem, Ramsey theory, Eulerian graphs and, very often, the Erdős-Rényi model of random graphs – is an active, rapidly-growing field that is still being developed. Extremal graph theory is conflagration of not only deep, complex, cutting-edge mathematical theory but also urgent, necessary and practical applications.

Maria Axenovich

Growing up in Novosibirsk, Russia, Maria Axenovich was exposed to mathematics early. At age six she was conducting combinatorial arguments on her daily trips to the bakery—figuring out which set of coins to use to purchase bread.

Around age 10, Axenovich began learning several programming languages. "In grade school there were a lot of algorithmic studies and projects," she recalled. "For example, when I was in the 4th grade, I had to write a training program for younger kids to teach them how to take a measurement with a thermometer." Later, during a summer project in her mother's lab at the Institute of Cytology and Genetics, she wrote a program to analyze pedigrees used to study the inheritance of diseases like scoliosis.

Living just minutes away from Novosibirsk State University and Sobolev Institute of Mathematics allowed the high-schooler to become involved with courses and research activities on campus. While attending a seminar one evening, a project on series-parallel graphs caught her eye and she began working to solve the posted problem. Axenovich found working on graphs with Sergey Avgustinovich as an advisor very inspiring. It was then she began to think of herself as a mathematician.

"I think it is very difficult to make a significant improvement on serious problems using methods from one discipline only. Many great results of graph theory used techniques from other fields. So, it is important to take a broader view of things." –Maria Axenovich

"I think there is a very deep connection between graph theory and analysis that people have only recently (say, in the last 4 years) started to discover, even though the tools that we've had to figure it out have been around for 30 years or more.

Graph theory in particular and combinatorics in general are about discrete things—things you can count; analysis is about continuous models, such as motion.

It has always been assumed that calculus (analysis) doesn't appear to be of much use in graph theory. But I think it is, in a very fundamental way—and this is important. It's more than solving a problem, it's like setting up a whole new theory. I think viewing graph theory in this new way will enable us to solve problems that we could never hope to solve before, and may reveal interesting problems we did not previously see." –Ryan Martin

Ryan Martin

His love of the game led 8-year-old little league catcher Ryan Martin, to pick up a copy of *Bill James' Baseball Abstract.*

James published the baseball abstract with pages of statistics from the early history of the game to the prior season. He attempted to rank baseball players and even predict the outcome of a season based on prior statistics. The detailed lists of statistics and sometimes very elaborate formulas were intended to grade a player's value and performance.

"For example, he created a simple formula called Runs Created," Martin recalled. "I'd use the formula from the 1980 abstract and then calculate the value for players after the 1981 season before the new abstract came out." This early use of baseball statistics grew into a study called "sabermetrics," which every major league team now uses to assess future talent.

Martin found that once he understood the formula and the reasons for it, the outcome didn't intrigue him so much. Fortunately, in 7th grade he started algebra, giving him more interesting things to think about and harder problems to solve.

Martin thinks that for most mathematicians, the goal is to solve problems. "For me the greatest joy is the accomplishment in solving the problem; it is really like a puzzle," he explains. "For most math research, you know what the answer ought to be (the picture on the box), but the pleasure is in putting it together."

Combinatorial *matrix theory* research group

The simplest relationship between two variables x and y is a linear one, i.e., we can write $y = a\ x$, where a is some number. The graph of this relationship is simply a straight line through the origin. If the actual relation between x and y is more complicated, say $y = f(x)$, one can often get a first impression by linearizing the function f at a point (say x^*), i.e., by computing the derivative $f'(x^*)$, and by looking at the straight line through the corresponding point $(x^*, f(x^*))$ with slope $f'(x^*)$. This is the basic idea of first year calculus!

If the variables have more than one component, a linear relation between them is given by a matrix. Consider, e.g., x_1 to be the value of a share in an S&P 500 index fund, and x_2 to be the value of a share in a NASDAQ stock market index fund (these values change with the stock markets). Suppose you inherit an investment of a_1 shares in the S&P 500 index fund and a_2 shares in the NASDAQ index fund (and in this example you do not change the number of shares you own). Then your total wealth from these two investments is $y = a_1 \cdot x_1 + a_2 \cdot x_2$, a linear relation with two variables (the values of the shares x_1 and x_2) on one side, and one variable (just y) on the other side. The matrix here is given by $(a_1\ a_2)$. In general, a linear relation between n x-variables $x_1,\ldots,x_n$ and m y-variables $y_1 \ldots,y_m$ is called a system of linear equations, and is given by a matrix with m rows and n columns. Just as in the one-dimensional case, linearizing a function $y = f(x)$ yields the so-called matrix of partial derivatives (Jacobian matrix), an object studied carefully in Calculus III.

Because of their description of linear relationships, and because of the information that can often be gained by linearization, matrices are virtually everywhere in mathematics and in applications to statistics, natural sciences, engineering, social sciences, etc. In this way, many problems in applications become problems in matrix theory (also called linear algebra). Several interesting subdisciplines have gained substantial attention lately, such as 'combinatorial matrix theory.'

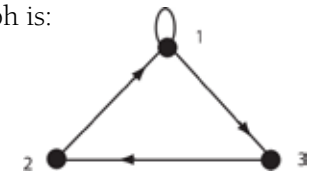
Combinatorial matrix theory does not study an m x n matrix with its numerical entries, but looks at certain patterns of the entries, e.g. their sign (positive, zero, negative): The sign pattern of

$$\begin{pmatrix} 4 & 0 & 2.1 \\ -3 & 0 & 0 \\ 0 & 17.3 & 0 \end{pmatrix}$$

is the matrix of the signs of the entries, i.e.,

$$\begin{pmatrix} + & 0 & + \\ - & 0 & 0 \\ 0 & + & 0 \end{pmatrix}$$

The study of such 'sign matrices' is very valuable in many areas of applications, e.g., in economics where often the sign of a variable is known (and important), but the exact value is not necessarily known. A square (i.e., n x n) sign matrix can be associated to a (directed) graph, i.e., a mathematical object consisting of vertices (one for each of the numbers 1 to n) and arcs between them (one for each nonzero entry in the matrix). The graph of the sign matrix above has arcs representing the entries (1,1), (1,3), (2,1), and (3,2); a picture of this digraph is:



Interestingly enough, some convincing results about sign matrices can be obtained by studying the associated graph.

Leslie Hogben works in combinatorial matrix theory, using techniques from linear algebra, combinatorics, graph theory and other areas of discrete mathematics and algebra to understand pattern matrices. Currently she works in two main areas of combinatorial matrix theory, 1) eventually nonnegative matrices and their sign patterns, and 2) the minimum rank, maximum nullity, and zero forcing number of a graph.

Nonnegative matrices are those whose entries are all nonnegative. They play a crucial role in many areas of mathematics and sciences since they describe specic dynamical

Hogben enjoys mentoring undergraduate research groups during the summer.

systems through the model $x_{m+1} = Ax_m$. Here x_{m+1} and x_m are variables with n components, A is a n x n matrix, and m denotes a time instant, $m + 1$ the next time instant. The interesting question is: What will happen to x_m as m becomes large? Many models in the natural and social sciences are of this form, and one would like to know if x_m approaches zero, or grows to infinity, or shows some other pattern. The key to this problem is understanding the behavior of A^m, which comes from the simple observation that $x_{m+1} = Ax_m = A \cdot (Ax_{m-1}) = A^2x_{m-1} = \ldots = A^{m+1}x_0$, where x_0 is the initial value for the variable under consideration. Eventually nonnegative matrices are those for which all entries are nonnegative starting at some product A^m for some m (even if this time instant m is very large). An example of such a matrix is $A = \begin{pmatrix} 1 & 1 \\ 1 & -0.1 \end{pmatrix}$, for which we have $A \cdot A = A^2 = \begin{pmatrix} 2 & 0.9 \\ 0.9 & 1.01 \end{pmatrix}$ that is positive; one can show that A^m is positive for all $m \geq 2$. Hogben and co-authors have described sign patterns for which all matrices having that pattern are eventually positive, and have introduced a subclass of eventually nonnegative matrices that has mathematically 'nice' properties.

The nullity of a matrix A is the number of independent solutions x to the system of linear equations $Ax = 0$. The maximum nullity problem for a graph is to determine the maximum nullity of the family of matrices whose nonzero pattern is described by the graph. For a fixed size of matrix, higher the nullity means the matrix carries less information. High nullity matrices are important in applications because they can be easier to work with. For example, in the study of communication in computer science, it is desired to find high nullity matrices that describe the transfer of information between computers, thereby minimizing the amount of information that must be exchanged.

For a (directed) graph with each vertex initially colored either black or white, apply the color change rule that if a vertex has an arc to exactly one white vertex, then that white vertex changes color to black. The zero forcing number of a graph is the smallest number of vertices needed to be initially colored black so that repeated applications of the color change rule will result in all vertices being black. The zero forcing number provides an upper bound to the maximum nullity of a graph. From a combinatorial matrix perspective, this is how zero forcing number arose, to study the minimum rank/maximum nullity problem. But independently, physicists began to study what they call graph infection, another term for applying the color change rule. Graph infection is used to study control of quantum systems. Hogben and her students and other coauthors have obtained a variety of results on minimum rank and zero forcing, and are sharing results with the physicists working on graph infection.

Hogben founded and leads the Combinatorial Matrix Theory Research Group. Pictured here is a group from Summer 2010.

Leslie Hogben is the author of 50 journal articles, an associate editor of the journal *Linear Algebra and its Applications*, the editor-in-chief of the reference *Handbook of Linear Algebra*, and the secretary/treasurer of the International Linear Algebra Society. A major focus of Hogben's work has been the enhancement and diversication of the US mathematical workforce by doing research with undergraduate and graduate students. Less than half the mathematics PhDs granted by US universities are earned by Americans, and this is regarded as a serious national problem by the National Science Foundation (NSF). Furthermore, African Americans, Latinos/Latinas, and women are under-represented in the mathematical workforce, wasting a pool of talent. Research experience as an undergraduate (or early graduate student) and the personal mentoring by a faculty member that occurs in this work have been shown to play an important role in increasing interest among undergraduates and retention among doctoral students, especially students from under-represented groups. Hogben directs the Department's NSF-funded summer research experience for undergraduates (REU). She is a leader in early graduate research (EGR), having run a research group for many years that included early graduate students and developed the department's EGR course. She has mentored 24 undergraduates in research and 16 graduate students though the Combinatorial Matrix Theory Research Group, EGR course and summer research programs for graduate students, in addition serving as the major professor for 3 students who have earned a PhD and 3 current doctoral students. She strives to build research connections with faculty at colleges and universities that emphasize undergraduate teaching, and has 10 faculty collaborators at such institutions.

Using differential equations to understand and improve electric power system behavior

Things that move are often called 'systems', such as stars, cars, blood in vessels, stock prices etc, and they are mathematically often represented using 'differential equations'. These are mathematical models that describe the current state of a system and its tendency for change. E.g., describing a car that travels down main street we note where the car is right now, together with its velocity and acceleration (in a specific direction), and we can predict quite accurately where the car will be in a few seconds from now. By the way, the 'differential' actually comes from 'derivative' as we learn it in calculus.

Of course, the actual behavior of a system usually depends on the many influences that act on it. Going back to the car example, this includes road parameters (such as surface roughness), weather (such as wind speed and direction), position of the car accelerator and the brake pedal, the position of the steering wheel and many others. Some of these parameters cannot be influenced by the driver (wind, potholes), others can (accelerator, brake, steering wheel). Some of these influences are rather random (weather, size and frequency of potholes), others are natural constants (gravity acting on our car).

All in all, we end up with a system description that has at least a few 'differential equations' with fixed or random parameters, and some control inputs that we can use to make the system do what we would like it to do (such as steering a car). The analysis and design of such systems is at the heart of my mathematical research. Here 'analysis' means that we try to understand what behavior the system will display, and 'design' means that we try to come up with parameter values, input channels etc that allow us to control the system in the way that it is intended to function. Mathematically, this is a combination of control theory, dynamical systems theory, and the theory of random processes. My main area of application is national infrastructure, in particular large electric power systems.

Described by colleagues as "a superb teacher at every level of the professorate," Kliemann thoroughly enjoys teaching. Also during his tenure, Kliemann has consistently encouraged research activity and development of research programs and ideas, and acted as a change agent for both educational and economic development outreach programs.

Electric power systems are large interconnected systems of generators, lines, and loads (or users). The dynamic (or time varying) behavior of these systems is described by large systems of (several hundred) coupled 'differential equations', with controls used to keep the power supply reliable and stable throughout the country. From 1993 to 2001 I worked with Aziz Fouad and Vijay Vittal (both members of the National Academy of Engineering) on developing nonlinear methods for power systems stability design, resulting in over 25 papers and reports. These methods have since been adopted by the IEEE (Institute of Electrical and Electronic Engineers); compare the 2005 IEEE Committee Report *Inclusion of Higher Order Terms for Small-Signal (Modal) Analysis* by the Task Force on Assessing the Need to Include Higher Order Terms for Small-Signal (Modal) Analysis. This technology is making its way into software and control settings at the largest utility companies in the US and Canada.

We have recently begun to analyze electric power systems for which the random influences are modeled explicitly. While loads (consumer behavior) always had a random character (the utility company does not know when you go home and turn on your lights), these stochastic models have become more important with the recent emphasis on renewable energy sources: many of these resources themselves follow random dynamics (wind, waves, sun, …) that need to be incorporated into the power systems that use these sources. Together with a group of mathematicians, electrical engineers and statisticians (in Chile and the US) we are developing new methodology and software to understand reliability and stability issues of electric power systems under random perturbations – with the hope (and expectation) that this will lead to better system design principles that can be used some day by the utility industry.

Kliemann's research interests encompass the areas of dynamical systems, stochastic differential equations, and control theory and their intersections and application to diverse scientific questions. Among his more "pure" mathematical contributions, Kliemann is known for his contributions to "deterministic dynamical control" and "asymptotic analysis of stochastic differential equations."

Kliemann is also known for his ability and interest in interpreting theoretical work in terms of applications. In particular, in work with a variety of researchers across quite different fields such as neuroscience, mechanical engineering, electrical engineering and statistics, Kliemann has addressed aspects of the growth of nerve cells in the brain, reliability in mechanical systems, and electrical power network analysis.

Currently Chair of the Department of Mathematics, Kliemann is the author or coauthor of 90 refereed publications, 15 books or chapters in books, 11 book reviews, 3 popular science articles

and has been principle investigator or co-pi on 22 research grants of various types ranging from grants to organize conferences to full-fledged research grants. His vita lists some eleven pages of plenary and invited lectures at international conferences, seminars and colloquia. He has been actively involved in building international programs in both graduate education and research.

After taking a course on numerical methods for differential equations Kliemann taught during his sabbatical at the Universidad Catolica de Chile, PhD student (Universidad de Chile) Humberto Verdejo wrote a paper with his major professor, Luis Vargas, and Kliemann which he then presented at NAPS in Calgery. Following this experience, Verdejo arranged to study with Kliemann at ISU for one year to develp an analysis for real power systems.

A mathematical paradigm for surgery as a cure for cancer

Cancer! The very word strikes terror into the hearts of those who are told that they or a loved one has it. It is not just a single disease for which one can obtain a preventive vaccination or treat with an antibiotic, but a family of diseases with various causes, genetic, environmental, or systemic such as the aging process itself. The longer one lives, the greater are the chances for biochemical miscues during natural cell replacement within the body. Indeed, statistically speaking, the older one is, the more susceptible one is to the disease.

One of the classical treatments for cancers which manifest themselves in tumor form is surgery. After removal of the offending mass, the patient will ask "am I cured?" or "Will it come back?" The surgeon's cautious reply is usually something like: "Well, we think we removed all of it, but we cannot be sure that it did not metastasize or spread to other organs or tissues. If it doesn't reappear after a few years, it probably did not metastasize and it is highly unlikely that it will return."

So, how does cancer spread? Why does one need to wait so long to be sure that the disease does not return? And why do some people remain disease free while for others the disease returns at some other site in the body?

Harvard scientist Bruce Zetter[2] proposed that the development of secondary tumors may be affected by behavior of the growth factors and growth factor inhibitors secreted by the primary tumor. We know that growth factors secreted from the primary tumor have a rather short half life and thus cannot diffuse very far without being degraded or deactivated, while growth factor inhibitors have a much longer half life and are thus able to diffuse over longer distances. This means that while the primary tumor is present, the growth factor inhibitors it secretes are more likely to impact potential nearby secondary tumors than the growth factors, keeping the area near the primary tumor free of additional tumors. When the primary tumor is removed, the impact of growth factors expressed by any very small secondary tumors present increases and additional tumors may appear.

Thirty days after the growth of a malignant tumor (left) is removed, while no secondary tumors were apparent, several appeared (right) within 5-7 centimeters from the excision site.[1]

In mathematically modeling this phenomenon, Boushaba, Levine and Nilsen-Hamilton[3] began by identifying a suitable set of biochemical players and an associated biochemical wiring diagram that describe how the activating agents expressed by the secondary tumor are suppressed by the deactivating or inhibitory agents expressed in excess by the primary tumor.

Next, the group turned the wiring diagram into a system of partial differential equations that describe the space and time evolution of the concentrations of the biochemical players and the sizes of the primary and secondary tumors. The system was then approximated by a system of twelve ordinary differential equations (a compartment model with six odes in each compartment coupled by the separation distance L between the tumors).

In comparing the extinction and growth times for the secondary tumor with and without removal of the primary tumor, the group found that proximity can play a significant role.

As you can see on the graph, for secondary tumors more than 11.7 cm from the primary tumor, with or without surgical removal of the primary tumor, the secondary tumor will grow. However, the growth will be faster (growth time smaller) after surgery than when the primary is present. Likewise, for secondary tumors less than 7.7 cm from the primary tumor, with or without surgical removal of the primary tumor, the secondary tumor will become extinct. However, the presence of the primary

tumor shortens the time of extinction.

It is within the window of distances between 7.7 cm and 11 cm from the primary tumor where the discussion around surgical removal of the primary tumor is most critical. In this scenario, the secondary tumor in this window will become extinct if the primary tumor is not surgically removed while it will grow to the size of the former primary tumor if the primary tumor is surgically removed.

The simulations illustrate that the size and location of this interval is very sensitive to the chosen values of the growth factor half life and the (latent) growth factor inhibitor half life (the jagged appearance of the curves is a numerical artifact).

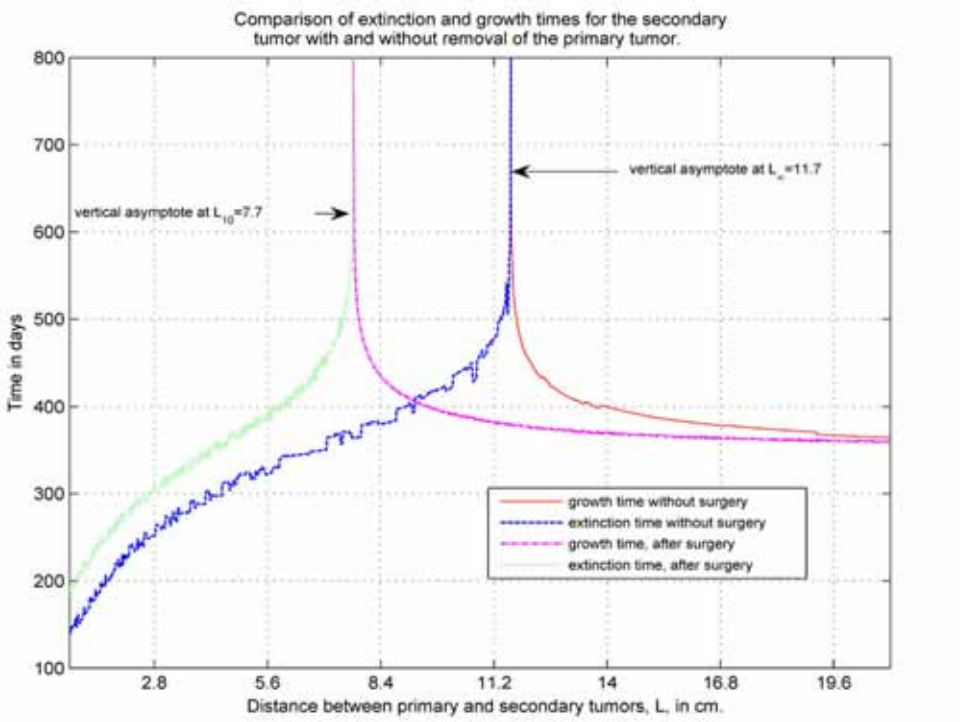
The simulations illustrate that the size and location of this interval is very sensitive to the chosen values of the growth factor half life and the (latent) growth factor inhibitor half life.

It should be noted that the scale of time suggests that the model overestimates the time at which the secondary tumor will be visible (300 to 500 days instead of 30 to 50 days). There are several reasons for this. First, as remarked above, the results are very sensitive to the half lives of the key players. The values used are taken from in vitro measurements while the tumor illustrated is clearly an in vivo observation.

Moreover, transport of the molecular players here was assumed to be only by diffusion, a relatively slow process. Transport by convection cannot be excluded because the ambient pressure in tumors is known to be larger than the ambient pressure in the surrounding tissue (one of the reasons chemotherapy is such a traumatic cancer treatment). This pressure head is responsible for accelerating the transport of the molecular players from the primary to the secondary tumor.

The model we propose here is only one possible explanation for the growth of secondary tumors after the surgical removal of a primary tumor. It has been suggested that perhaps the growth of secondary tumors was promoted by a large number of factors produced during wound healing following surgeon's resection. This is also possible. However, most of the growth factor induced by the surgeon's knife would be at or very near the wound site. This wound induced growth factor should induce secondary tumor growth very near the wound site and not remote from it as is observed. Moreover, in order for there to appear secondary tumors at a more remote distance from the primary tumor site, there must have been some secondary tumor cells at that remote site to begin with unless some mutational events occurred in consequence of the resection.

A more detailed report of this study[3] is available online at *www.math.iastate.edu/pdfs/LevineMathMatters.pdf*.



Results reveal two vertical asymptotes; one at 7.7 cm and the other at 11.7 cm. (The jagged appearance of the curves is a numerical artifact.)

[1] V. De Giorgi, D. Massai, G. Gerlini, F. Mannone, E. Quercioli, and P. Carli, *Immediate local and regional recurrence after the excision of a polypoid melanoma: tumor dormancy or tumor activation?*, Derm. Surgery, 29 (2003), pp. 664-667.

[2] B. R. Zetter, *Angiogenesis and tumor metastasis, review,* Ann. Rev. Medicine, 49 (1998), pp. 407-22.

[3] K. Boushaba, H. A. Levine and M. Nilsen-Hamilton, *A mathematical model for the regulation of tumor dormancy based on enzyme kinetics,* Bull. Math. Biol. 68(2006), pp. 1495-1526.

Howard A. Levine (Math) and Marit Nilsen-Hamilton (Biochemistry, Biophysics and Molecular Biology)

Dedication, collaboration and enthusiasm are Liu's equation for success

Hailiang Liu's general research interests lie in the area of computational and applied mathematics. Liu is particularly interested in the combination of analysis and numerical methods for the resolution of multiscale problems arising in various scientific fields such as fluids, gases, plasmas and polymers. Partial differential equations (PDEs), the governing equations that quantify physical phenomena, are the common framework in his research. Liu's work has involved several PDEs which include hyperbolic wave equations, kinetic transport equations, and Schrödinger equations.

Hyperbolic wave equations

Hyperbolic wave equations are mathematical models to describe wave motion in daily life. For example, light waves and acoustics waves are governed by linear wave equations. These have applications in geosciences, seismology and medical imaging. Nonlinear hyperbolic conservation laws are to describe shock waves arising in gas motion, the solution is extremely important for the design of airplanes that are stable in turbulent air.

Kinetic equations

Kinetic equations play a central role in many areas of mathematical physics, from micro- and nano-physics to continuum mechanics. They are an indispensable tool in the mathematical description of applications in physical and social sciences, from semi-conductors, polymers and plasma to traffic networking and swarming. The ultimate goal of Liu's NSF Focus Research Group (FRG) is to develop novel analytical and numerical methods based on kinetic descriptions of complex phenomena with multiple scales and with a wide range of applications.

Schrödinger equation

Fundamental in quantum mechanics, the Schrödinger equation describes the quantum state of physical systems in time. It is as central to quantum mechanics as Newton's laws are to classical mechanics. It is a wave equation in terms of the wave function which predicts analytically and precisely the probability of events or outcomes. The detailed outcome is not strictly determined, but given a large number of possible events, the Schrödinger equation will predict the distribution of the results.

Conferences organized by Liu are typically well attended, as was the Midwest Numerical Analysis Day (above) held this past April on the ISU campus. Liu sees such events as opportunities to remain current and build potential collaborations.

A typical project

In one of his current research projects, Liu is working to develop a recovery theory of high frequency wave fields, as part of the National Science Foundation-funded FRG (Focused Research Group) project on *Kinetic description of multi-scale phenomena: theory, computation and applications*.

In the computation of wave propagation, when the wave field is highly oscillatory, direct numerical simulation of the wave dynamics can be prohibitively costly and approximate models for wave propagation must be used. The conventional ray method will be adequate if the field of rays at no point loses it regularity. In realistic problems we virtually always have to deal with caustics, where rays concentrate and the predicted amplitude by the ray method is unbounded and hence unphysical. Recovery of high frequency wave fields beyond caustics has long been a challenging problem.

Ability to get information from a specific equation

Gaussian beams are asymptotically valid high frequency solutions to wave equations, concentrated on a single curve through the physical domain. Superpositions of Gaussian beams provide a powerful tool to generate more general high frequency solutions that are not necessarily concentrated on a single curve. The accuracy of Gaussian beam superpositions in terms of the wavelength is essential for the recovery theory, and was thought a rather difficult problem decades ago. With collaborators, Liu has developed a systematic construction of Gaussian beam superpositions for a large class of wave equations subject to highly oscillatory initial data, and obtain the optimal error estimates in the appropriate norm. The obtained results are valid for any number of spatial dimensions and are unaffected by the presence of caustics.

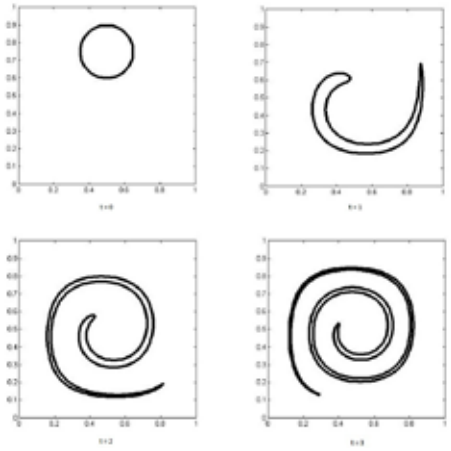
Indeed, there are many cases where a wave motion is highly oscillatory, like light waves, and computing these can be very time consuming. Beams turn out to be very efficient for resolving these situations, creating enormous potential for applying Liu's recovery theory to diverse applications.

Mentoring student researchers

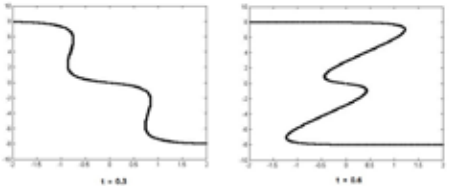
Currently, two graduate students, Hui Yu (below, left) and Nattapol Ploymaklam (right), are working on Liu's NSF-funded FRG project.

Yu's research focus is on development of entropy satisfying methods for kinetic models of polymers (see images below).

Ploymaklam studies fast algorithms for recovery of high frequency wave fields, for which a fast level set algorithm is essential (see images above, right).

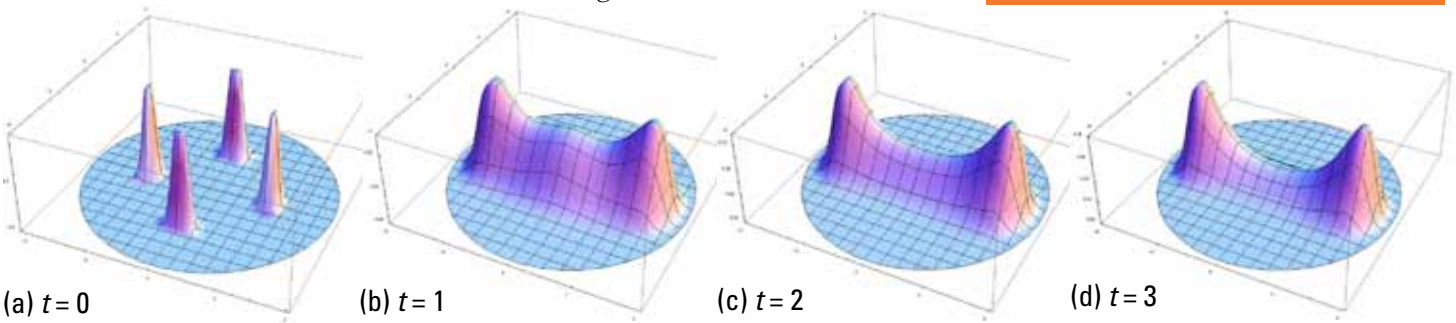


This image shows the evolution of a circle placed in a single vortex flow. The time required for the numerical simulation is reduced by a factor of 10 or more while maintaining the same accuracy.



These images show multivalued velocities of the semiclassical limit of the Schrödinger equation. The time required for the numerical simulation is reduced by a factor of 20 or more while maintaining the same accuracy.

The Dio L. Holl Chair of Applied Mathematics, Liu possesses a rare combination of expertise in analysis, numerical methods and physics. These are talents that promise potential collaborations with researchers in science and engineering. Liu has had continuous support from the National Science Foundation, and has made significant and substantive contributions to such diverse areas as critical threshold dynamics, alternating evolution methods, level set closure of kinetic equations and recovery of high frequency wave fields.



(a) $t = 0$ (b) $t = 1$ (c) $t = 2$ (d) $t = 3$

These images illustrate the capacity of the entropy satisfying method to quickly capture the equilibrium distribution of polymers when the initial distribution is concentrated at four isolated points.

Number theory: Solving the mysteries of numbers

Number theory - the study of numbers, in particular, whole numbers - is one of the most sophisticated branches of mathematics.

From the time of the Greeks, many great problems in number theory have fascinated mathematicians, and motivated the developments of many fundamental theories.

Nowadays, number theory has also become an applicable science and has seen applications to physics, chemistry, biology, computing, engineering, coding and cryptography, random number generation, acoustics, communications, graphic design and even music and business (see, e.g., the book *Number theory for computing* by Song Y. Yan, Springer Verlag, 2002 (2nd edition)). For instance, many public-key cryptography schemes that provide internet security use number theory e.g. the RSA Cryptosystem, or elliptic curve cryptography.

About 400 years ago, Pierre de Fermat wrote down on the margin of a book that the equation $X^n + Y^n = Z^n$ has no integer solutions when $n > 2$, unless X or Y or Z are 0. Since then, finding solutions to this so-called Fermat's Last Theorem has inspired many generations of mathematicians and mathematics amateurs. It is like a marvelous destination described by Marco Polo which inspired explorers like Columbus to adventure to new continents. In 1993, Andrew Wiles at Princeton announced that he had a found way to validate Fermat's ingenious claim. To outsiders, this ended the haunt of Fermat's spirit; to the insiders, Wiles' noble proof brought another fundamental revolution to mathematics.

Wiles approach, built on the recent advances in algebra, geometry, number theory, and topology (the study of the properties of curved spaces that are preserved through deformations, from which we can tell the fundamental differences between apples and donuts), created powerful tools suited for cracking the some well-kept secrets of mathematics. His approach opens the door to many influential programs and philosophies initiated by mathematical giants like Jean-Pierre Serre (who won the two highest honors in mathematics: the Fields medal (the 'Nobel Prize of Mathematics'), and the Wolf price) and Robert Langlands (another Wolf prize winner).

Ling Long's main research interest lies in number theory, especially arithmetic geometry - the study of arithmetic using algebra, geometry, topology, et al. Modular forms are functions on the complex numbers that satisfy certain functional equations (or symmetries). The theory of modular forms, therefore, belongs to the area of complex analysis, but it also shows up in combinatorics and string theory in physics. Most importantly, the theory of modular forms has been the central focus of number theory during the past century, and its importance is manifested in the crucial role this theory played in the proof of Fermat's Last Theorem.

A profound program called 'dessin d'enfants' ('child's drawing' in French) was proposed by another mathematical titan, Alexander Grothendieck, in 1984. These 'drawings' of simple graphs connect properties of complex functions to certain surfaces and symmetries of these surfaces. In this setting, modular forms essentially catch the relations between different surfaces that

are linked by the 'drawings'. Therefore, 'dessin d'enfants' gives a nice explanation why modular forms arise naturally in many settings, sometimes natural sometimes totally unexpected. In reality, modular forms are also used to build models for efficient communication networks.

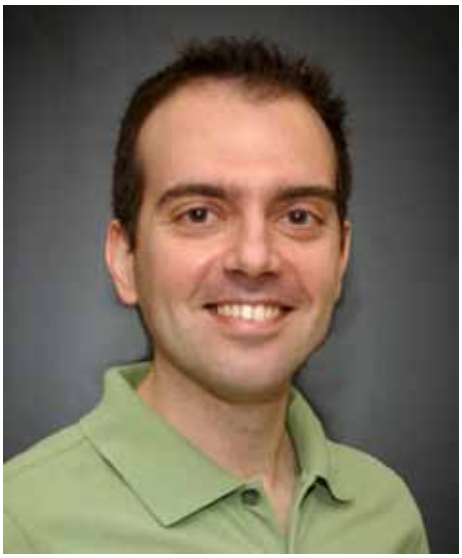
Among all modular forms, there is a special class called congruence modular forms whose symmetries can be described according certain 'modulo n' arithmetic on the numbers. The theory of congruence modular forms is well-developed due to a nice machinery called Hecke theory and continuous efforts of mathematicians including the Indian genius Srinivasa Ramanujan, Erich Hecke, and Pierre Deligne, another Fields Medalist. However, noncongruence modular forms, i.e. modular forms not in this special class, remain mysterious. As a matter of fact, the majority of modular forms are noncongruence and it has become clear that noncongruence modular forms deserve a thorough study especially from the view point of 'dessin d'enfants'.

In late 1960's Atkin and Swinnerton-Dyer initiated a serious study of noncongruence modular forms using an ingenious empirical and theoretical combined method, and major developments in this direction were made by Scholl. Ling Long's interest in noncongruence modular forms was ignited by her earlier work on arithmetic geometry, and much of her excitement for the area comes from the Atkin-Swinnerton-Dyer and Scholl approaches. During the past few years, she has made several breakthroughs to long standing open problems in this area and gradually developed a research program with increased outside recognition. One of her fascinating projects is to understand a mysterious and intriguing link between noncongruence modular forms and automorphic forms, a generalization of congruence modular forms, in the framework of Langland's philosophy which governs Wiles' proof of Fermat's Last Theorem. Some of her work, such as characterizing the arithmetic behaviors of noncongruence modular forms, has applications to the conformal field theory that is important in physics. Currently, Long's research projects are supported by the National Science Foundation. Ling Long's vision is to lay down a fundamental framework for the theory of modular forms in general which can be applied to other disciplines.

Ling Long loves to work with motivated students and has an extensive research network. She works with collaborators at Cambridge, Cornell, McGill, Penn State, Purdue, the University of Illinois at Chicago, and elsewhere on papers and proposals. Long also actively mentors female mathematicians. One of her projects on modular forma involved three junior female number theorists at other institutes.

Long (left) and colleague Richard Ng (right) visit with now AMS president George Andrews after his presentation on the mathematical genius of Ramanujan. Long was instrumental in bringing Andrews to campus to give the Miller Distinguished Lecture.

Mathematical modeling using differential equations takes guesswork out of live tissue transfer



Mathematics is playing a role in efforts by plastic surgeons to ensure success of live tissue transfers from one part of a person's body to another.

In the first published quantitative model of tissue transfer, physicians and mathematicians have teamed to ensure tissue segments chosen for transfer will receive enough blood and oxygen to survive.

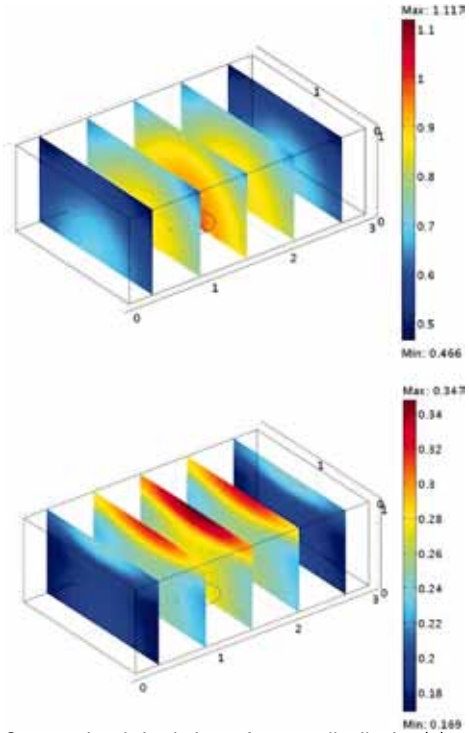
Anastasios Matzavinos, assistant professor of mathematics at Iowa State University, said research, which uses differential equations, has shown mathematics can take the guesswork out of such transfers. Matzavinos and mathematicians and plastic surgeons from Ohio State University have developed mathematical models of the blood supply and oxygen in tissue segments. The modeling could reduce failures in reconstructive surgery.

Matzavinos is one of the authors of the study published in the July 21, 2009 edition of the *Proceedings of the National Academy of Sciences*. The research is supported by the National Science Foundation.

Tissue transfers are often used to rebuild body parts damaged by disease or injury, such as the reconstruction of a patient's breast following cancer surgery. In this example, a plastic surgeon will cut away a segment of the patient's tissue, often from the lower abdominal area, and reattach it to restore the patient's breast.

The removed tissue, called the flap, is fed by perforator vessels, a vein and artery that travel through muscle to support skin and fat. Matzavinos said surgeons believe the vessels must be at least 1.5 millimeters in diameter to provide oxygen flow to sustain the flap.

In earlier procedures, physicians removed the skin and underlying muscle. The more-invasive procedure resulted in abdominal immobility



Computational simulations of oxygen distribution (a) in artery blood and (b) in tissue after four hours of tissue reperfusion in the case of a small rectangular tissue flap.

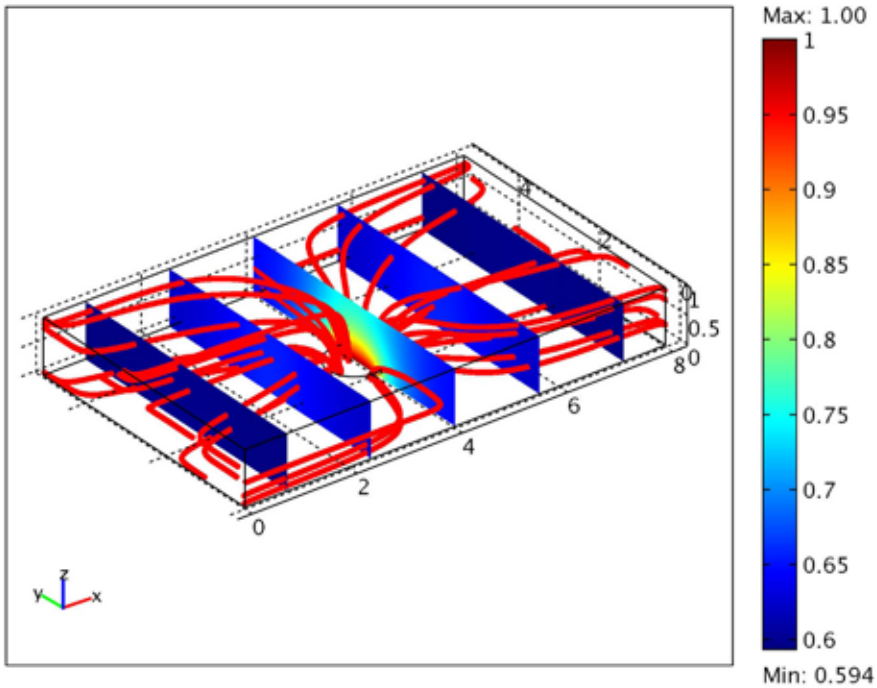


Figure showing a computational simulation of the distribution of arterial blood pressure and the corresponding pressure streamlines within a small rectangular tissue flap. The pressure streamlines indicate blood-flow trajectories.

and loss of strength. Surgeons now routinely take only the fat tissue and the vessel. However, because the muscle is no longer transferred, the diameter of the vessel must be the correct size to provide enough blood for the flap to live.

"Right now there is no medical protocol for this," said Matzavinos. "Surgeons only use their experience and trial and error.

If we know more about the relationship between the size of the perforated blood vessels and the size of the tissue flap to be transferred, the surgeries will be more reliable."

If the initial blood oxygen levels in the transferred tissue are not at least 15 percent of the corresponding levels in blood, according to the study, the tissue farthest from the vessels will begin to die. This results in additional surgery and sometimes the entire procedure must be redone.

Matzavinos said measuring the blood flow through small vessels and the thousands of tiny capillaries is the challenge. "We don't know the exact vascular structure of the tissue," he noted. Researchers, however, developed a way to average the oxygen concentration of the capillaries.

The mathematical model uses three values: the average oxygen concentration in the capillaries, the rate of exchange from vessels to tissue and the pressure under which the blood is flowing through the vessels.

Five differential equations provide a range between the flap size and the needed diameter of the vessels.

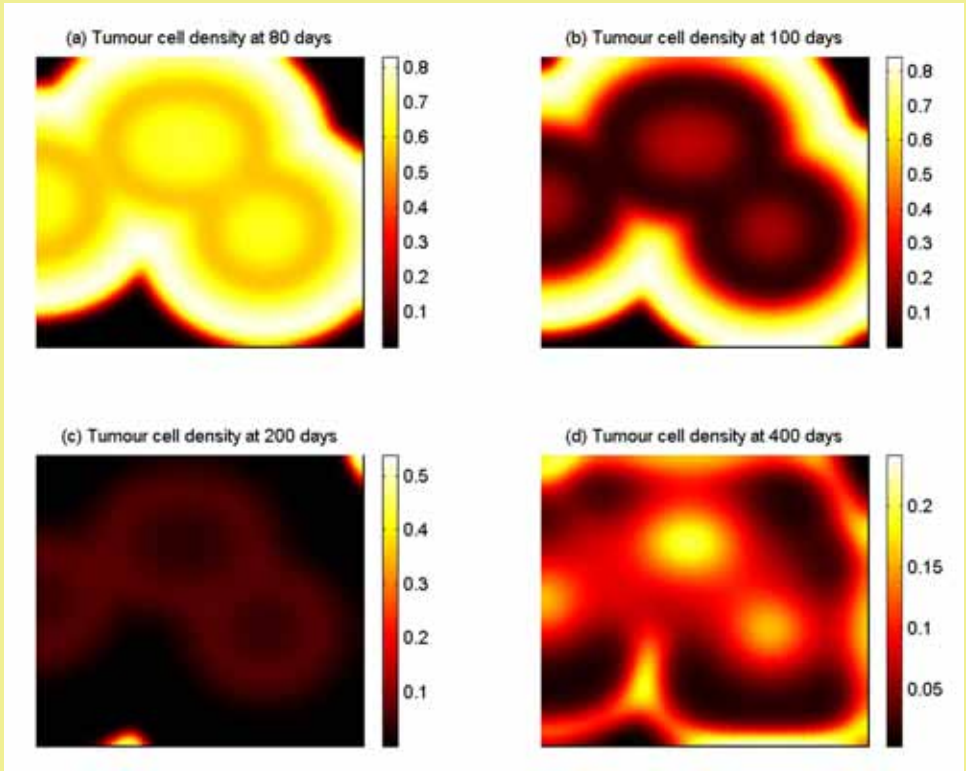
"This is a new predictive tool that can provide consistent results for physicians," Matzavinos said.

The mathematical model is still under development and will need to be tested. However, Matzavinos is confident it can someday be part of an imaging and software package that will provide surgeons with reliable data on the likelihood of survival of transferred tissue.

The need to interpret and extract possible inferences from high-dimensional datasets has led over the past decades to the development of dimensionality reduction and data clustering techniques.

Scientific and technological applications of clustering methodologies include among others bioinformatics, biomedical image analysis and biological data mining.

So-called fuzzy clustering methods are often used in the study of high-dimensional data sets, such as microarray and other high-throughput bioinformatics data. A fuzzy clustering algorithm, DifFUZZY, which utilises concepts from diffusion processes in graphs and is applicable to a larger class of clustering problems than other fuzzy clustering algorithms has been developed by Anastasios Matzavinos, Sijia Liu and colleagues from the University of Oxford in UK and Lincoln University in New Zealand. The algorithm has been implemented in Matlab and C++ and is available at: *www.maths.ox.ac.uk/cmb/difFUZZY*



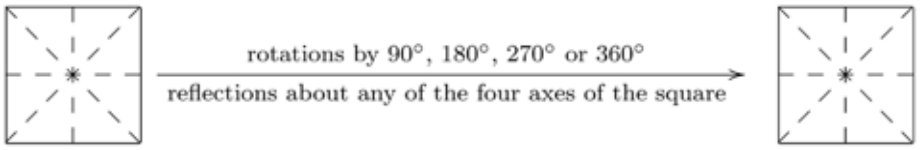
Matzavinos' research in computational biology spans a diverse range of topics and biological systems. The figure above shows computational simulations of solid tumor growth in the presence of an immune system response. Numerical predictions of such computational models make it possible to comprehend the mechanisms involved in the appearance of spatio-temporal heterogeneities detected in solid tumors infiltrated by cytotoxic lymphocytes.

Hopf algebras and modular categories: Mathematics of symmetry in nature

The sense of symmetry is a natural instinct of mankind, and the appeal of symmetry has been a guidance for understanding nature since the dawn of science. The symmetry of geometric objects can be easily visualized but it may not be obvious to formulate in a theoretical language which provides a foundation for further investigation. The "hidden symmetry" of a physical system is generally unlikely to be recognized unless that kind of symmetry has been studied or understood in a certain form. These theoretical understandings of symmetries have been provided by the mathematics culture since the beginning of human civilization.

The concept of *group* began to take shape in the 19th century in the course of studying the symmetry of polynomial equations. However, the application of group theory to molecular symmetry in inorganic chemistry, and to elementary particles in high energy physics was not discovered until the twentieth century. These historic interplays between mathematical symmetry and science have provided powerful testimony for the scientific importance of algebraic structure in mathematics.

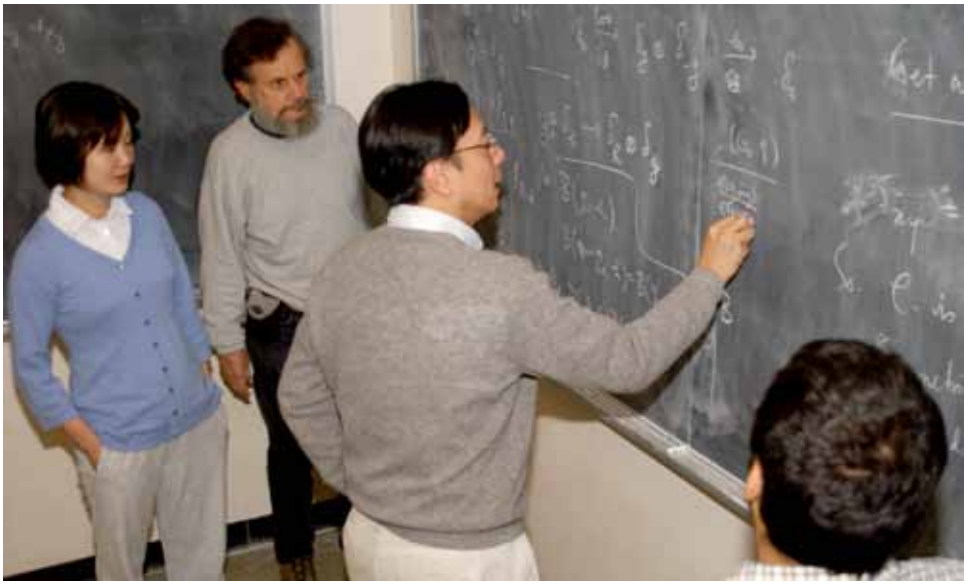
The symmetry of a geometric figure or the symmetry of a 3-dimensional *regular* array of points can be described by the collection of *rotations* and *reflections* which leave the figure or the array appearing to be unchanged. To illustrate this kind of symmetry groups, one can consider a square locating in a plane:



If one rotates the square by 90º, 180º, 270º and 360º about its center, the square appears to be unchanged. The four rotations form the cyclic group $\mathbf{Z}_4$ and this group describes the rotational symmetry of the square. If one allows to flip over the square, then the reflections about any of the four axes of the square will also leave the square appearing to be unchanged. These eight operations form the group D_4 which describes the symmetry of the square considered in our 3-dimensional space.

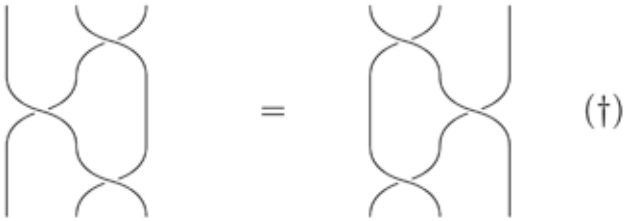
The concept of group is a mathematical abstraction of the symmetries of geometric figures. *Hopf algebras* can be viewed as generalized groups, and they were originally introduced by Heinz Hopf in algebraic topology, a branch of mathematics which studies the spatial properties that are preserved under continuous deformations of objects. *Modular categories* are algebraic structures that arise naturally in rational conformal field theory, which is a branch of mathematical physics concerning elementary particles, the fundamental constituents of matter. One important relation between Hopf algebras and modular categories is that the latter can be constructed from certain Hopf algebras.

It was realized lately by



A gathering of the Representation Theory Seminar. Ng (at board) and colleague Tathagata Basak started the seminar in an effort to better understand modular categories and their relations to different branches of mathematics and physics.

physicists as well as mathematicians that Hopf algebras can be used to describe the symmetries of some physical systems. To illustrate this point, one can observe the equality of the following link diagrams:



The second diagram can simply be obtained by pulling down the middle string and moving up the first string of the first diagram. Let us simply write an invertible matrix σ for the single braid  and the identity matrix id for a single string  . If any of these diagrams are put together horizontally, we simply equate the diagram with a certain product $\otimes$ of the associated matrices. (To be precise this product is called the *tensor product*–its explanation would be a bit lengthy in this context.) If one diagram stacks on the other, then we equate the diagram with the multiplication of the associated matrices. In this convention, we have:

$\mathrm{id}\otimes\sigma =$  and $\sigma\otimes\mathrm{id} =$ 

The above equation (†) of links becomes the algebraic equation:

$$(\mathrm{id}\otimes\sigma)(\sigma\otimes\mathrm{id})(\mathrm{id}\otimes\sigma) = (\sigma\otimes\mathrm{id})(\mathrm{id}\otimes\sigma)(\sigma\otimes\mathrm{id})\,.$$

The equation is called the *quantum Yang-Baxter equation* (QYBE) which arises in statistical mechanics. Obviously, not every invertible matrix σ satisfies the QYBE, and obtaining non-trivial solutions for this equation is well known to be very difficult. However, it was discovered by Fields medalist Vladimir Drinfel'd that each Hopf algebra can systematically generate an infinite family of non-trivial solutions of the QYBE.

Ng (center) joins other participants at the international conference on Vertex Operator Algebra and related topics in talking about some questions of modular categories of certain vertex operator algebras.

Siu-Hung Ng's present research interests lie in the area of Hopf algebras, modular tensor categories, and some of their invariants called Frobenius-Schur indicators.

His research program has been continuously funded by the National Security Agency or the National Science Foundation since he joined Iowa State University.

The philosophy of his research in part is to understand our nature via mathematics. More importantly, his research contributes to the foundation of mathematics which is a building block for future scientific discoveries.

This introduction only partially reveals how these mathematical structures interplay with sciences and symmetries in nature. In-depth understanding of these subjects is yet to be discovered.

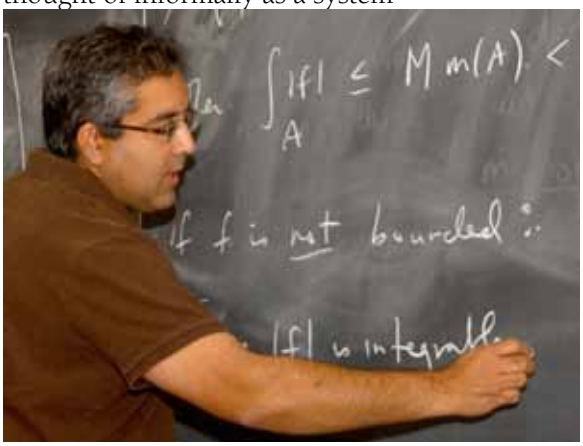
Structure, dynamics, flow, growth, behavior and more

Sunder Sethuraman's research over the past few years has included understanding the structure and dynamics of various models of traffic, fluid flow, real world network growth, quenched or rapidly cooling behavior, and other phenomena, from the point of view of statistical physics and random processes. Here, Sethuraman writes about some contributions to the modeling of three of these systems as well as collaborations with faculty and students.

Traffic and fluid flow.

A basic concern in applications is to describe the behavior of an individual component as it interacts in complex ways with many others. In the context of fluid flow, this might be to ask what sort of trajectories does a spot of oil take in a sea of water. Or, can one understand the asymptotic motion of a single car navigating traffic on a network of roads?

Since some sort of measurement error is assumed present, and since it's often intractable to follow all the interacting components, one frequently models the systems probabilistically. In other words, the motion will possess some stochastic variability, and can be thought of informally as a system of random walks where walker components execute moves by observing their environment—the other components—and then making a random displacement. In such models, it is useful to view the distinguished particle, or tracer particle in certain time and space scales, that is much forward in time from a very high vantage point. Our main results are to characterize the tracer motion in these scales as some sort of continuum diffusion process or Brownian motion, that is a type of random motion with continuous paths, with parameters determined by the type of interaction in the system.



Sethuramun lectures graduate students in real analysis.

One impact, then, of this sort of description is that one can effectively follow the tracer motion in terms of its continuum limit. In another vein, this sort of limit picture can be seen as a form of justification of the use of diffusions in applied physical modeling, a fundamental concern in statistical physics since Einstein's 1905 seminal paper introducing Brownian motion.

Real world networks.

Recently, following the explosion in data collection in many networks, such as friend or social networks, biological networks, the internet, genealogical trees, etc., there is now, computationally, an understanding of the structure of these networks. As has been well reported in the media, such networks seem to consist of a few hubs connected to a majority of nodes with only a few connections, the so-called small world phenomena. A theme identified in the growth of such networks is that a node with a large number of connections is more likely to increase its connectivity than a node with few links. This is sometimes referred to as a preferential attachment rule where a rich node tends to become richer.

In one project, with Iowa State colleagues Krishna Athreya and Arka Ghosh, we have constructed a probabilistic model, in terms of branching processes, of a general network growing by preferential attachment. Through this model construction, one can recover a celebrated law of large numbers, or in other words a precise form of the mean behavior, for the number of nodes with a given number of links, and explain it in more natural terms. But more importantly, one can understand other statistics of the network from this construction such as the typical connectivity of a fixed node, or the node with the maximum links.

Time-inhomogeneous processes and quenched dynamics.

In some physical observations, such as tornado occurrences and glass formation, for instance, which are

time dependent, it is natural to use a time-inhomogeneous Markov chain to model the evolution over time, at least to first order. In such chains, or sequences, the next state depends only on the current time and state of the system, and in particular not on the past motion up to the present location.

Inhomogeneous processes are much less understood than their homogeneous cousins where the next step depends only on the current state but not the current time, which are computationally easier. In particular, standard applied and theoretical concerns, such as the central limit theorem, which state that errors from the mean can be explained in terms of a bell curve, are not well understood in inhomogeneous chains. In this respect, part of our theoretical work has been to give and explain a sharp condition on when a central limit theorem is valid. The impact of such a result is that one can classify data in many applied time-inhomogeneous models as being typical or an outlier with confidence.

We have also investigated the large deviations in inhomogeneous chains, that is the probabilities of rare events. From an applied view, computing such probabilities are quite important, as understanding how catastrophes and quite unexpected scenarios develop is essential to model analysis. As an example, our large deviation results shed light on the quenching dynamics of glass formation where a very hot material is cooled rapidly so as to form a glass. Glasses are quite interesting, and still an object of interest and some mystery, as they lack a regular structure associated to a solid. One can think of a glass as being matter in some sort of locally optimal, but disordered state, somehow chosen among many such states in the cooling process. The large deviations established quantify the chance of atypical cooling, and show how typically the material can persist out of an optimal state in the quenching process.

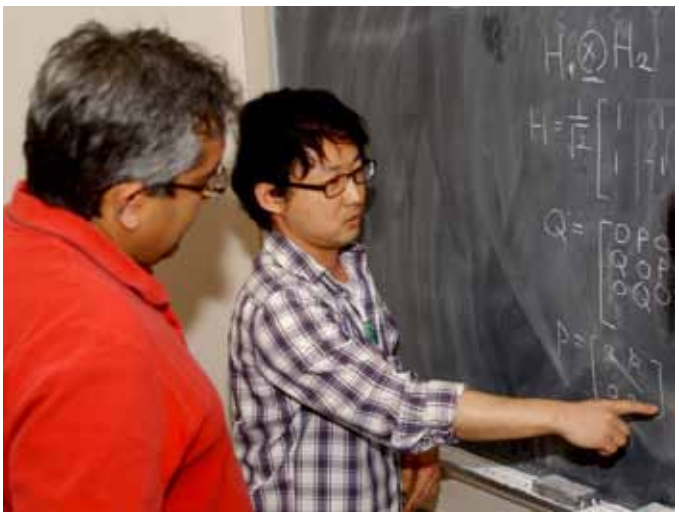
Jihyeok Choi reviews research with Sethuramun.

Collaborators and students.

It has been a pleasure to work with interesting collaborators, both at home and around the world, mostly Rio de Janeiro, Paris, Bangalore, New York and Cincinnati, as well as talented students.

One of the pleasures of mathematics is that it can be done most any place, and often the strongest collaborations occur outside usual academic halls. In particular, in the age of e-mail, it is now normal to conduct mathematical conversations in text, a case in point being a recent collaboration between a colleague in Budapest, one in Bangalore, and myself where at no time were all three of us in the same place.

I have had the privilege of working with very good students both in mathematics and statistics, and enjoy this type of collaboration quite a bit. Often, together we have embarked upon new fields, as was the case with time-inhomogeneous chains, and real world networks. Also, sometimes students have worked on more established projects. Discussing research with students has certainly been a high point in these years.

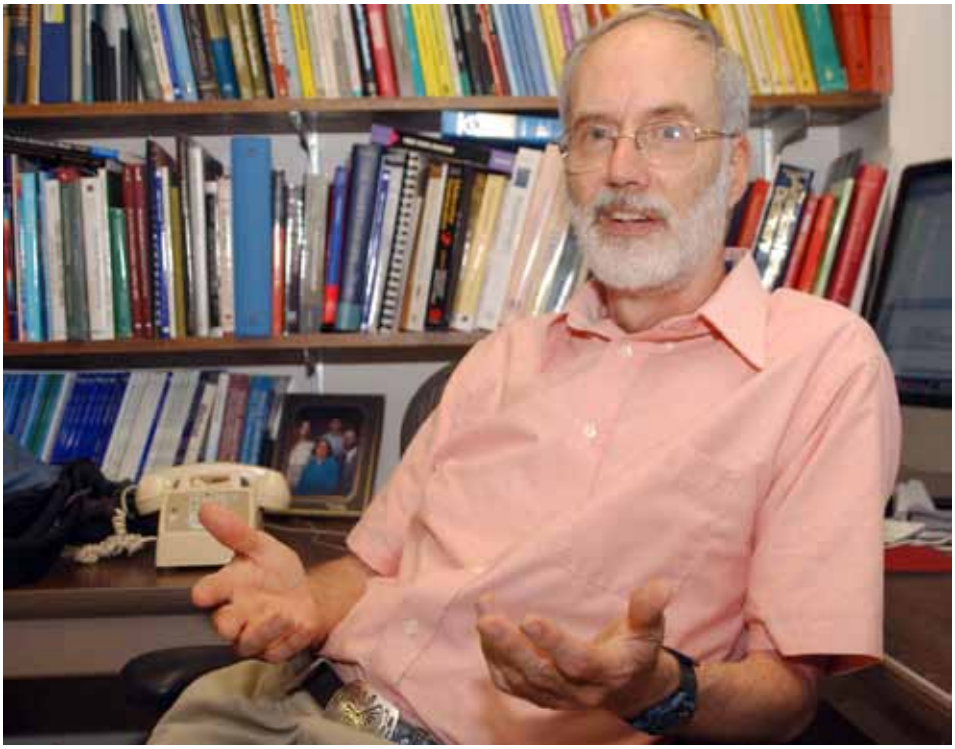


Youngsoo Seol discusses a problem with Sethuraman.

Sethuraman focuses on probability theory, specifically with respect to some interacting particle systems. He is also interested in random media, random graphs, random walks, time-inhomogeneous models, among other things. His research is continuously supported by National Science Foundation and National Security Agency grants.

Sethuraman received the 2008 Prix de l'Institut Henri Poincare for best paper in *Annales de l'Institut Henri Poincare Probabilites et Statistiques*, and in 2009 was awarded the Lambert Faculty Award by the Department.

The *continuing evolution* of Stephen Willson



Janson Professor of Mathematics and University Professor Stephen Willson enjoys discussing mathematics with students and colleagues.

These days, University Professor Stephen Willson's work focuses in the mathematics of biological evolution.

Darwin's Theory of Evolution suggests that species of animals and plants gradually accrue modifications. With time, new species occur. A diagram showing the relationships among certain species is called a phylogeny or a phylogenetic graph. The public commonly sees these in museums of natural history, for example showing relationships among the dinosaurs or among mammals.

Willson's research concerns methods of building phylogenetic graphs, usually from the DNA of extant plants and animals.

Until recently, almost all phylogenetic graphs were thought to be "trees" in the mathematical sense. That is, the branches never grew back together. Increasingly it has been found that events like hybridization and lateral gene transfer are important.

For Willson, taking the possibility of these events into account, the diagrams become "networks" rather than "trees." His recent research focuses on methods of building and interpreting these networks that are not necessarily trees.

Willson saw that generalizing this concept from trees to networks presented a challenge: if it was too general, there would be no interesting theorems; if it were too specific, it would not apply to real problems.

While Willson's research is application-driven, the results can be stated in purely mathematical terms.

"Biologists work to discover aspects of the history of the evolution of species. It has recently become clear that hybridization and lateral gene transfer are important phenomena that have greatly influenced this history; they had previously been ignored," said Willson. "My work tries to understand some of the implications for the mathematics behind these reconstructions."

The integration of mathematics and biology is a natural development for someone who started out studying to become a medical doctor only to learn that he was, in fact, a mathematician.

An undergraduate in science, Willson was studying to become a medical doctor when he discovered the beauty and utility of mathematics. During freshman and sophomore chemistry and physics classes, Willson recalls, "I observed that the most interesting parts were where the most mathematics was utilized to explain what was happening. I thought that the way mathematical structures illuminated a subject was very beautiful as well as useful." While most of his friends

did not share his vision of mathematics, it was enough for Willson to change the course of his future.

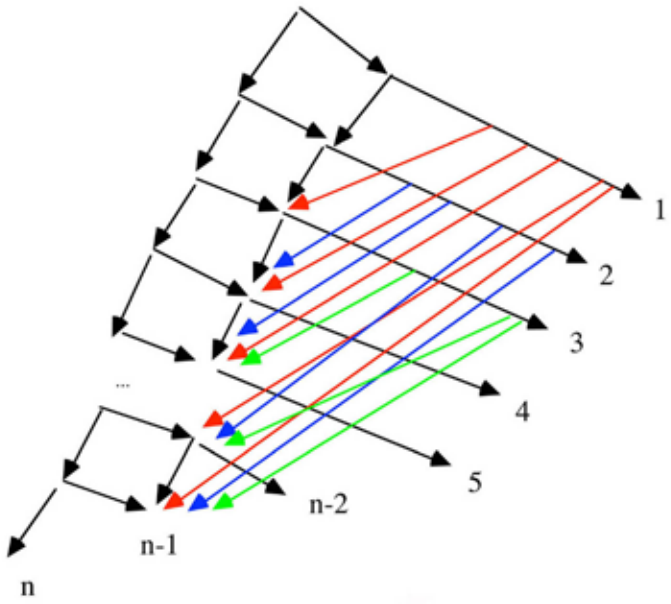
Forty-four years later, Stephen Willson still finds mathematics illuminating.

It was an interdisciplinary seminar established in the mid-90's by former ISU professor Jim Cornette that piqued Willson's interest in phylogenetics. Faculty members from different departments shared basic ideas and described techniques for many applications of mathematics to biological subjects. Willson found that he had some ideas about phylogenetics that were new and potentially useful.

"To be an effective teacher, you need to be sensitive to the level of the student you are addressing. Too detailed an answer will lose some students and be inadequate for others. When a student comes to office hours, the student should work each step if possible; I must resist the temptation to work the problem for the student, but instead give the smallest possible hint when the student gets stuck. Often it is hard to recognize the step that stops them."

"People repeatedly ask whether mathematics is a discovery or an invention. I think that the practice of mathematics is both. Once the definitions are set, a mathematician discovers relationships. Part of the art of mathematics, however, is inventing the exact definitions that fit the situation. In mathematical biology, there are vague ideas that need to be made into precise definitions. Giving precision is a kind of invention. The goal is precision (invention) that permits interesting theorems (discoveries)."

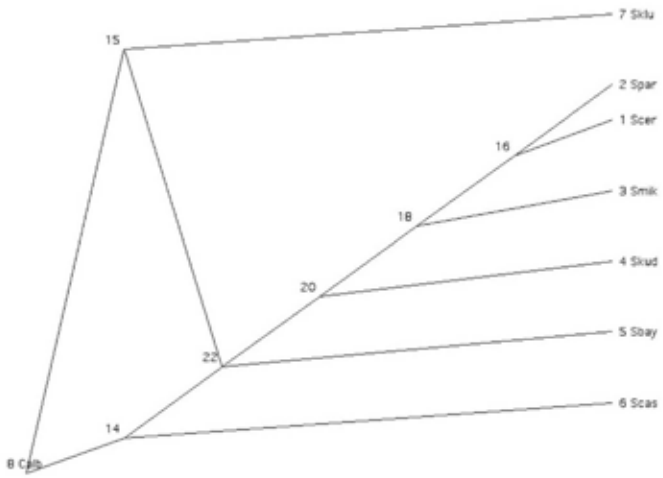
"A display of currently existing species may reveal peculiarities such as the fact that whales and dolphins are more closely related to cows than to horses. How do we know that this is true? What does it really mean? These are questions about phylogeny."



Willson has explored the possible complexity of networks representing hybridizations that satisfy simple hypotheses.

Lateral gene transfer is any process in which an organism incorporates genetic material from another organism without being the offspring of that organism

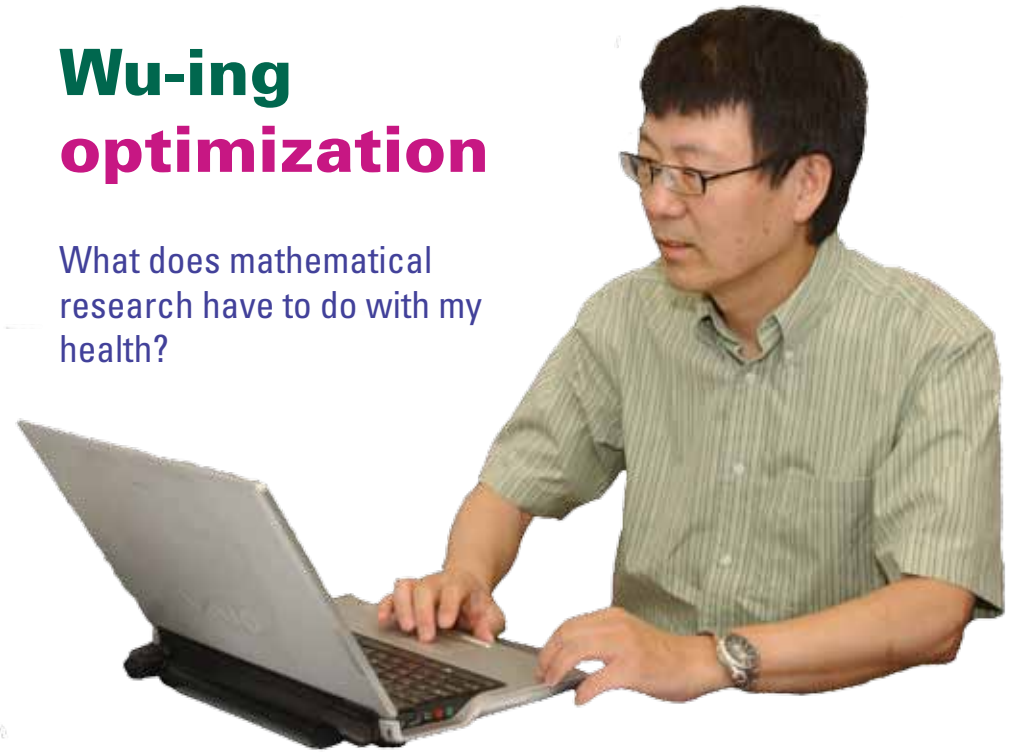
Hybridization is an event where viable fertile offspring arise from parents of different species



Willson has written software which can detect potential hybridization events from the DNA of extant species.

Wu-ing optimization

What does mathematical research have to do with my health?



Growing up in China, Zhijun Wu was 12 years old when persistent respiratory problems kept him out of school for an entire semester. Instead of falling behind, Wu found his interest as well as his ability in mathematics blossoming as he studied independently. Devouring exercise after exercise on his own, he advanced to the point that upon returning to class, he was asked to tutor all the other students in mathematics. It was the quiet beginning of a fascinating professional career.

Over his 20 years of research experience with engineers and scientists, Wu says he finds mathematics everywhere.

"Mathematics is such an important field. A common tool for all the scientific fields, it builds the foundations for many disciplines such as physics, chemistry, mechanics, and even some social sciences such as economics, psychology, and linguistics.

Optimization

Wu's interdisciplinary research in optimization and its applications, particularly its applications in biology, has afforded opportunity to collaborate with many biologists, biochemists, and biophysicists.

In this field of applied mathematics, the goal is to find an optimal solution among all possible solutions to a mathematical, engineering, or science problem where the standard is defined by a mathematical function. "For example," Wu explains, "if we are looking at the profit a company can earn, then the optimal solution will be the one that maximizes the profit."

Wu says many engineering and science problems are formulated as optimization problems, as they want to decide some of the variables or parameters so they can optimize certain values of their systems.

"Optimal means not only maximizing benefits but also minimizing some harms," Wu adds. "Put all these together, we still have an optimization problem – optimization for all concerns."

In his work with optimization Wu focuses on mathematical and computational biology. In particular, he studies the microscopic biology of protein modeling and the macroscopic biology of evolutionary dynamics.

Protein modeling

Proteins allow biological systems to work at all levels: chemical reactions, metabolism, moving, digesting, thinking, etc.

Studying proteins and their functions—those supporting life or causing disease—help researchers understand biological systems.

Hundreds of thousands of proteins in biological systems form certain structures that perform biological functions or transport biological ingredients.

Determining the structure of a protein helps find its most stable state and understand its biological function. Mathematics and computation allow Wu and his team to identify the 3D structures of proteins.

Using data from nuclear magnetic resonance (NMR) Wu's team can find the structure for a protein that best fits the experimental data such as the distance data (between pairs of atoms).

The problem of finding the positions of the atoms of a protein given the atomic distances or their ranges is called the distance geometry (DG) problem and is nontrivial to solve, for there are usually tens of thousands of atoms in a protein, while the distance data is not complete and contains errors. An efficient, accurate, and biologically meaningful solution to the problem is always a great challenge to obtain.

With support from NIH and

NSF, Wu's team has developed a linear time algorithm for the solution of the DG problems with exact distances and a least-squares approximation algorithm for the problems with inexact distances. They have also formulated a new class of DG problems called generalized DG problems for modeling structures with distance intervals. An optimization algorithm has been developed and tested for the solution of the generalized DG problem.

Mad Cow, HIV and more

Two particular proteins that Wu has been developing methods to solve structures for are the prion protein that causes Mad Cow disease and HMV1, which helps the HIV virus infect its host.

Determining the structure of the prion protein, Wu explains, helps understand how it changes and causes Mad Cow Disease, while finding the structure of the HMV1 protein, will assist researchers in designing drugs to destroy its 3D structure and hence its (bad) biological function.

Evolutionary dynamics

The process where individuals adapt and species evolve to survive—for better or worse—from generation to generation is called evolutionary dynamics. At times, elements like viruses or bacteria may cause systems to change or evolve in very short time periods.

To model how biological systems evolve and illustrate their eventual steady state, Wu uses evolutionary game theory.

"In evolutionary game theory, species compete for resources," Wu explains. "In the end, some survive and some become extinct."

One particularly common outcome in game theory is a special steady state known as Nash Equilibrium.

Originally developed for solving mathematical problems in economics, the Nash equilibrium occurs when the players work with their strategies and eventually reach a state where winning and losing average out. In economics this is called market equilibrium.

Biological systems also reach the Nash Equilibrium after certain time period.

Mathematical models allow researchers to compute and predict the final equilibrium of a biological system.

"While models allow us to predict which viruses will go away ultimately, and which bacteria may be able to sustain," said Wu, "they also help us understand how the systems evolve."

Protein geometry databases

Wu's team has also developed protein geometry databases for atomic and residue level distance and angle distributions. Available online at *www.math.iastate.edu/pidd* and *www.math.iastate.edu/prtad*, the databases provide statistical information on various structural elements (distances or angles) derived from known protein structures. The information can be used to analyze, classify, and refine protein structures.

Wu explains a problem to a student in his differential equation class.

To young people interested in mathematics, Wu advises:

Broaden your view of mathematics to include classical subjects as well as new developing fields. The impact mathematics can make in sciences and society is exciting.

For young people challenged by mathematics, he offers:

While mathematics may challenge you, remember that it is very useful to your life and career. As reading helps us to obtain knowledge, mathematics helps us to think.

Mathematics is necessary to compete and advance in modern society.

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