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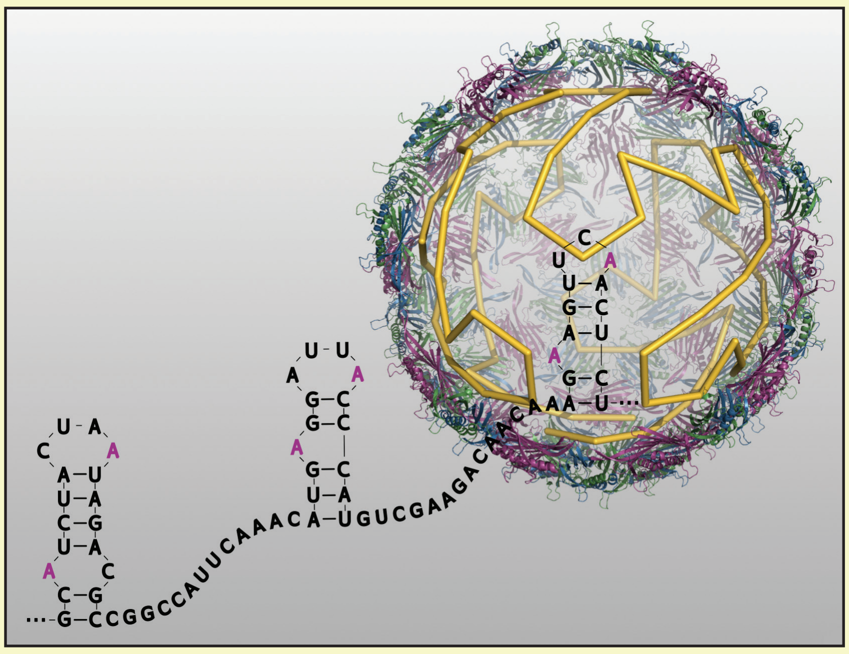
Life Sciences Special Issue

Check out articles from the SIAM Conference on the Life Sciences—and more—in this ***special issue****!*



In an article on page 3, Reidun Twarock describes the use of mathematics to study the formation, evolution, and infection rate of viruses.

Figure 1. *The Hamiltonian path representing genome organization in proximity to the MS2 capsid is shown in yellow inside a crystal structure of the capsid, together with a genomic fragment containing packaging signals (PSs) identified in [3]. The core sequence motif, the two As shown in magenta, is very sparse, demonstrating why sequence analysis alone is not sufficient to identify these PSs. Image credit: Richard Bingham, adapted from a figure by Tom Keef.*

Algorithmically Defining Olfactory Responses in Animals

By Bard Ermentrout

For their survival, animals use olfaction (their sense of smell) to locate food, find mates, and avoid predators. While animals excel at these tasks, the algorithmic and mechanistic processes governing this behavior are not well understood. Our lack of understanding is made vivid by the pre-industrial nature of current odor source localization technology; we use dogs to search for contraband, pigs to find truffles, and pouch rats to detect land mines.

While animals exhibit a wide range of morphological and physiological characteristics, they use similar cues to locate odor sources: differences in odor concentration across space and over time, measurements of local concentration gradients, frequency of odor encounters, and environmental cues about flow direction, such as wind or water flow. Moreover, animals share many morphological and kinematic similarities in their olfactory systems, including bilateral sensors, dynamic sampling behaviors (sniffing, antenna movements), and common anatomical features (neural circuitry in the first stages of olfactory processing). These commonalities suggest that convergent evolution has identified robust strategies for locating odors in complex environments.

Finding odor sources is hard because odor environments are complex. Odors in natural environments travel along turbulent flow paths governed by wind, topography, and molecular diffusion. What exactly does the odor landscape look like? Figure 1a (on page 2) shows an odor plume imaged by our collaborator, John Crimaldi (University of Colorado). It's clear that the concentration is far from being uniform or smooth in space. Locations near the source at some instants of time show nothing, while even distant places show bursts of high concentrations. Figure 1b (on page 2) displays the output from a photoionization detector (PID) at different distances from a line of odorant placed on a table in a room. Unlike the plume, the only airflow is the ambient turbulent flow arising from ventilation, movement, etc. in the room. Presumably, this is what a mouse perceives when trying to locate an odor trail. In the PID measurements, the baseline is higher near the source than away from it. But another common feature of these complex odor landscapes is that the rate of fluctuation increases with proximity to the source.

See **Olfactory Responses** *on page 2*

Biofluids of Reproduction: Oscillators, Viscoelastic Networks, and Sticky Situations

By Debbie Sniderman

Despite the introduction of millions of sperm into the female mammalian reproductive tract, fewer than 100 actually arrive at and penetrate the egg, enabling fertilization. A tenth of every ten million sperm reach the cervix, where they encounter a complex fluid environment containing embedded polymer structures. Only a tenth of those make it through the uterus. To reach the egg, the remaining sperm then must pass through the contracting oviduct. Oviducts are lined with mucosal folds and coordinated beating cilia that contribute to sperm transport. Some sperm may adhere to oviductal epithelia, requiring a change in their oscillation pattern to escape.

Mammalian fertilization involves many components, including sperm motility, female reproductive tract environment, biochemical signaling, and complex viscoelastic fluids. Successful reproduction in mammals relies on interactions of elastic structures with a fluid environment. Lisa Fauci (Tulane University) models these interactions using an immersed boundary (IB) framework to address fundamental questions about the biology of reproduction.

Why Biofluid Models Are Helpful

Sperm models help researchers understand various aspects of fertilization (see Figure 1). Sperm physiologists want to answer basic questions about the possibility of increasing sperm motility via treatment of chemical environments, which is beneficial to many industries.

Recognizing how non-Newtonian viscoelastic fluids help or hinder fertilization is also important. And a better understanding of how fertilized ova implant in the uterus can lead to improvements in in-vitro fertilization and clinical practices. For instance, should the injection of a fertilized ovum be timed with uterine contractions?

The rise of technologies such as microfluidic devices, labs-on-a-chip, and the ability to manipulate bacteria and flagellated organisms has triggered a surge in research activity surrounding the fluid dynamics of microorganism motility. For example, the creation of non-biological microrobots might facilitate drug delivery. Understanding how sperm deliver their payloads could help guide fabricated microswimmers towards tumors.

Fauci uses computational methods that couple both mechanical and biochemical systems with fluid dynamics in order to model fertilization and reproduction. As an alternative to continuum models, her group models a complex mucosal network as discrete nodes connected by viscoelastic elements. Using discrete networks is advantageous in that a network's connectivity can evolve to accompany structures' inhomogeneous material properties.

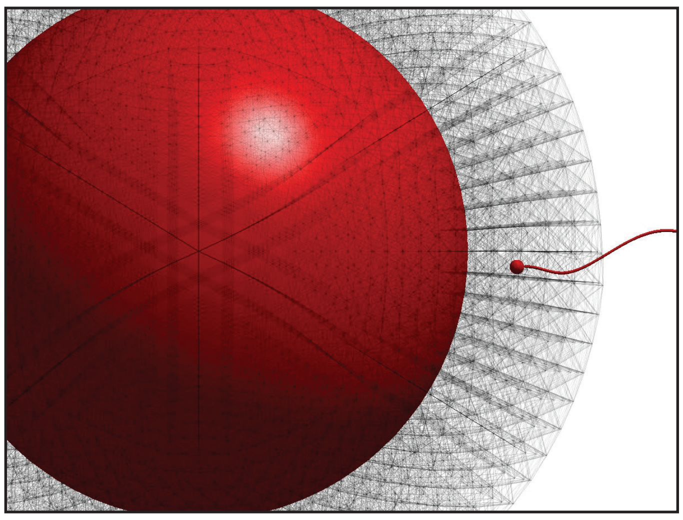


Figure 1. *Sperm-egg penetration model. Image credit: Jacek Wróbel, Julie Simons, Ricardo Cortez, and Lisa Fauci. To view a simulation, visit the online version of the article at sinews.siam.org.*

Motility: Beating Through Viscoelastic Fluids

Complex geometries, non-Newtonian fluids, and moving elastic and actuated interfaces all complicate sperm motility models. "Choices have to be made when choosing the types of models and what to include," Fauci says. Paraphrasing a famous quote by George E.P. Box, she adds, "All models are wrong, but some of them are informative."

Preliminary models, which initially looked at only one interface and one sperm or cilium, were 2D with simple domain geometries, like a periodic box rather than a more complicated pulsing tube. Researchers had to decide whether to use prescribed kinematic models of flagellar motion, or elastic rod models in which the flagellar shape emerges from the elastohydrodynamic coupling.

Elastic rod models assume that sperm flagella have tensile and bending energy that is minimized when the flagellar shape meets a preferred curvature. Forces derived from these energies also depend on stiffness coefficients. In models with biochemical properties, this preferred curvature is a function of the evolving calcium profile along the flagellum. Flagellar forces are coupled to a surrounding fluid. And at the microscale, inertia is negligible and Stokes equations are used. The coupled system is solved using the method of regularized Stokeslets.

Fauci's group also studies whether sperm gain any advantage by swimming through a polymeric network rather than a Newtonian Stokesian fluid. The model of a fluid coupled with an elastic network accounts for discrete links. It overlays a polymeric network onto a Stokes 3D fluid, with nodes

See **Biofluids of Reproduction** *on page 4*

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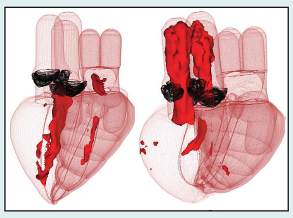
4 **Beating in Fluid: Hearts and Cilia by the Immersed Boundary Method**
Debbie Sniderman recaps an invited lecture by Charles Peskin at the SIAM Conference on the Life Sciences. In his talk, Peskin reinforced the versatility of the immersed boundary method, which is applicable to mathematical problems underlying two very different systems: hearts and cilia.



6 **Careers Outside Academia: How Should Math and Applied Math Students Prepare?**
Lalitha Venkataramanan, Rachel Levy, and Bill Kolata highlight themes from a career panel that they organized at the SIAM Annual Meeting. Takeaways for students and early-career individuals included an emphasis on mathematical maturity and programming proficiency at companies, and ways to acquire desirable technical expertise.

8 **Photos from the 2016 SIAM Annual Meeting**

9 **Computational Behavioral Ecology**
Debbie Sniderman outlines Tanya Berger-Wolf's plenary lecture from the SIAM Annual Meeting. Berger-Wolf's computational work uses data from a range of sources to provide scientific insight into the collective behavior of animals, pioneering the analysis of high-resolution data for behavioral science.

12 **Everyday Objects Make Applied Mathematics Tangible**
The 2016 I.E. Block Community Lecture emphasized the importance of touching, seeing, and feeling to central concepts in applied mathematics. Paul Davis gives us a vivid picture of Tadashi Tokieda's very palpable talk at the SIAM Annual Meeting.

11 **Professional Opportunities**

Olfactory Responses

Continued from page 1

Our group is using the behavior of animals in constrained environments to infer the algorithms they utilize to locate odor sources and follow odor trails. For example, in videos created by our collaborator Kathy Nagel (New York University), we observe fruit flies walking as controlled odors are turned on and off. The flies transiently make more frequent turns when an odor is switched from on to off. Nathan Urban (University of Pittsburgh), another collaborator on this project, films mice as they follow odor trails associated with a food reward. His lab finds that the mice are less accurate at following trails when one nostril (*naris*) is occluded, suggesting that "stereo-olfaction" may be important in trail following. The subjects in both of these experimental setups exhibit frequent movement called *casting*: the mouse moves its head around while sniffing or the fly moves orthogonal to the direction of the wind.

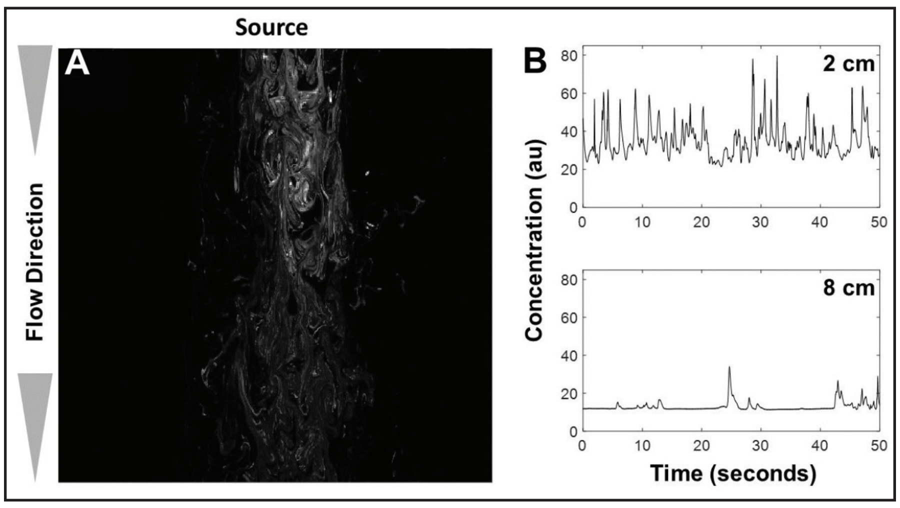


Figure 1a. *Snapshot of a chemical plume in water. Image credit: John Crimaldi.* **1b.** *Photoionization detector (PID) time series at 2 centimeters and 8 centimeters from an odor source. Image credit: Nathan Urban.*

We are currently using behavioral analysis to create models and test them on various odor landscapes. Testing the models in realistic settings is a challenge since we are just now beginning to understand what the landscape "looks" like to an animal. Approaches to modeling the odor concentration range from simple heuristic models to full Navier-Stokes simulations in controlled and closed environments. Any simulation of the environment should capture the intermittency of the odor, as seen in Figure 1. Furthermore, any navigation algorithm must be robust in the face of distortions of the plume, e.g., due to obstacles, changes in humidity and temperature, and sniffing or other movements of the animal itself. Once we have a good understanding of the algorithms, we want to then understand their neural and physiological basis. There is considerable knowledge of how odors are converted to electrical signals in the brain, but how these signals can be used for odor source localization remains a mystery. This article and a follow-up piece to appear in the October issue of *SIAM News* discuss a few of the simple algorithms that animals may use to find an odor source. Here I explore possible mechanisms for odor location that do not depend on the actual concentration.

Besides concentration, what other signals could be used to produce odor localization? Figure 1 shows rather clearly that the concentration fields are quite complex and chaotic. Figure 1b demonstrates that the frequency of fluctuations is much greater closer to the source; the plume in Figure 1a depicts similar behavior and a clear direction of the flow. These images suggest a method for finding the odor based on the frequency of odor encounters, and when possible, direction of the wind. For example, a very simple algorithm would move in a direction that shortens the intervals between odor encounters. An excellent algorithm, *Infotaxis*, is built with this premise in mind; the agent moves in a direction that increases the Shannon information [1]. At each time step, Infotaxis builds up an estimate of the probability that the source is at some location, $\hat{x}$. For instance, if the agent hasn't yet found the source, it is certain that the source is not at the current position. With this estimated probability, the agent estimates the entropy in each of the four cardinal points and moves to the point where the entropy is minimized.

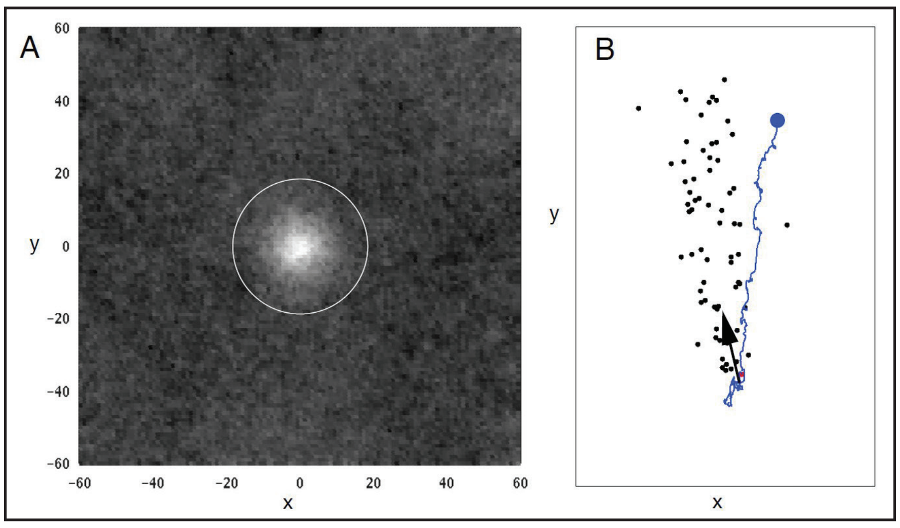


Figure 2a. *Fraction of time spent at different locations with a Gaussian odor source using the time between events.* **2b.** *A more sophisticated algorithm for a fly locating an odor in a "particle"-based plume. This shows the fly's track from the start (blue dot) and a snapshot of the "plume." Image courtesy of Kathy Nagel.*

While Infotaxis is an optimal strategy for finding an odor source when the encounters are rare, it is very computationally intensive. It is also not clear how a biological organism could implement Infotaxis. Instead, we have developed algorithms based on the rate of encounters between "spikes" of odor that work reasonably well in simple models for the odors. Since many odors arrive in a windborne plume, it is possible to use additional information about the wind direction to follow the odor upwind, and move crosswind or backwards when the odor is lost to increase the chance of finding it again. An example algorithm that does not use the wind works by keeping track of the last three odor encounters. If the time between those encounters is decreasing or the same, a possible strategy would be to continue to move in the current direction; otherwise, move in a random direction that is near the current direction.

For a very simple algorithm, this approach does reasonably well. Figure 2a shows the results of a Monte Carlo simulation of this algorithm applied to a single Gaussian source, which indicate that the agent spends much more time at the center of the source. Nagel has made careful observations of fly behavior in the presence of attractive odors. By temporally varying the on and off rates of an odor, she found a few rules that flies implement when walking in a small arena. Figure 2b shows an example simulation of her rules in the presence of a particle model for a plume. In this simple plume model, particles from the source are emitted randomly and drift/diffuse. A slowly-varying wind direction has a mean in the *y*-direction. The figure only represents a snapshot of the "plume" – if the fly is close enough to a particle, it registers as a hit. The rules use the wind direction as well as the frequency of on and off hits with the particles, and flies have a number of cells that register responses both when the odor is present and when it disappears. As with the spatial comparison algorithms, both of these temporal algorithms include a stochastic component when the hits become infrequent enough.

We are just beginning this work, and many mathematical and biological questions remain. How can we quantify and statistically imitate real odor landscapes in order to test models? What are the best algorithms for locating an odor and how do their parameters change at different spatial and temporal scales? What are the best search strategies when the odor is lost? Where in the olfactory system can the algorithms be implemented?

In a follow-up article to appear in the next issue, the author will describe mathematical aspects of tracking odors based on concentration difference, along with some aspects of foraging.

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Follow the Yellow Brick Road

Mathematics Reveals a Hidden Construction Manual in Viral Genomes

By Reidun Twarock

Viruses are a major public health burden. The continued emergence of viruses such as Zika and the large number of HIV infections worldwide are only two of many examples illustrating the urgent need for new, anti-viral solutions. Tackling this issue requires a better understanding of the mechanisms by which viruses form and infect their hosts.

Group, graph, and tiling theory can provide new insights into the architecture and formation of virus particles. Such insights are made possible by the highly regular geometric structures of the viral protein containers that encapsulate and thus provide protection to the viral genomes. In many viruses, these capsids resemble surface lattices with icosahedral symmetry, akin to Buckminster Fuller domes. We have developed group theoretical techniques to investigate the geometric constraints on such container architectures [7], and have shown that similar principles apply more widely in science, e.g. in fullerenes in carbon chemistry [1, 10]. We have also extended our tiling approach, Viral Tiling Theory, to assist experimentalists in understanding the geometries of self-assembling protein nanoparticles (SAPNs) [6]. The structural organisation of these particles, which are used to design Malaria vaccines, follow mathematical rules similar to those underpinning the assembly of virus particles.

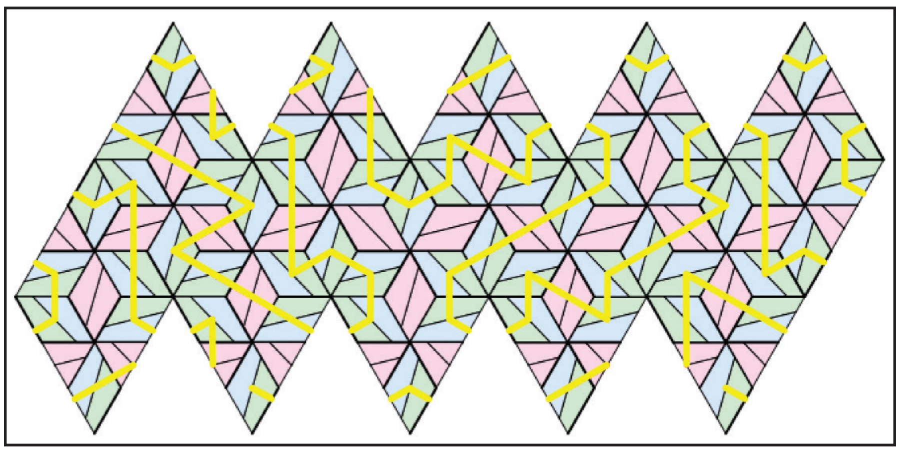

Figure 2. *A planar net representing the MS2 capsid architecture shows the location of the Hamiltonian path in Figure 1 with respect to the positions of the capsid building blocks, here represented as rhombs. Blue/green rhombs are in contact with PSs in the viral genome, and the yellow Hamiltonian path meets every such contact exactly once. Image credit: Richard Bingham, adapted from a figure in [5] by James Geraets.*

These structural models have paved the way for a major discovery that has fundamentally changed our understanding of virus formation. For decades researchers thought that viral genomes act like passive passengers in the formation of the viral capsids. Their impact on the formation process, if any, was attributed to electrostatics alone, triggered by the condensation of positively-charged capsid proteins on negatively-charged RNAs. Using mathematical insights, we have demonstrated that this view is not sufficient to account for the formation of single-stranded RNA viruses, a major group of viruses containing important human pathogens such as Hepatitis C, HIV, and the common cold.

The key to this discovery is rooted in combinatorial and graph-theoretical arguments exploiting viral geometry. The contact points between the encapsulated genomic RNA and the inner capsid surface act as the vertices of a polyhedron related in shape and symmetry to that of the capsid itself. The order in which the RNA-protein contacts are formed must correspond to a connected path visiting every vertex exactly once. Thus, the genome organisation in proximity to the capsid shell is topologically equivalent to a Hamiltonian path on this polyhedron (see Figures 1 (on page 1) and 2 (above)).

A classification of these Hamiltonian paths is a powerful tool in interrogating viral genomes for the existence of sequence-specific contacts between genomes and their capsids [3]. Such contacts are difficult to identify with bioinformatics alone due to the lack of any repeated, contiguous sequence motif of sufficient length in the genome, perhaps accounting for the long-held belief that any interactions between genome and capsid must rely entirely on electrostatics. Using our Hamiltonian paths classification, we showed that, by contrast, there is an ensemble of cryptic signals that vary around a minimal core sequence motif. These signals—which we termed packaging signals (PSs), in analogy to the single known specific contact previously identified by virologists—correspond to short, in many cases even disconnected, sequence elements presented in the context of specific types of RNA secondary structures, i.e. RNA shapes arising as a consequence of Watson-Crick base pairing (see Figure 1, on page 1). A striking outcome of this work is the conclusion that genome organisation is much more constrained inside viral particles than previously appreciated. Indeed, only a very small number of the possible Hamiltonian path organisations can actually be realized by a virus particle for geometric and combinatorial reasons. This initially-surprising result has subsequently fit excellently with cryo-electron microscopy data [5] (see Figure 3), corroborating this astonishing mathematical conclusion.

The variation around a minimal core sequence motif in the PS ensemble of a viral genome may explain why this hidden code has so long been overlooked. It also opens up the puzzle of how this code actually functions. To address the mechanistic implications of this code and provide an explanation for this variation in the recognition motifs, we used Gillespie-type algorithms to study the assembly of a dodecahedral shell as a proxy for a viral capsid [2, 4]. We monitored the assembly of the pentagonal building blocks in the presence of hypothetical RNAs, each with 12 PSs capable of binding to these assembling units. From a biophysical point of view, the variation of the PS motifs across the genome manifests itself in differing PS affinities for capsid protein. We therefore allowed the affinities of individual PSs in a viral RNA to vary between three settings, representing weak, intermediate, and strong interactions.

Interestingly, we observed significant differences in capsid yield for assembly around RNAs with distinct affinity distributions. The simulations alone could not explain why this was the case, but graph theory again was key in providing answers. We used Hamiltonian paths on the polyhedron representing all possible connections between neighboring binding sites—in this case an icosahedron—to classify different assembly scenarios. We showed that RNAs with better performing affinity distributions were organised inside the fully-assembled capsids via a very limited range of Hamiltonian paths. Translating these Hamiltonian path organisations into information regarding the geometries of the partially-formed capsids on the pathway to the complete particle showed that PSs act collectively to bias their geometries towards structures with larger numbers of protein-protein bonds. The hidden PS code thus acts as a construction manual for viral capsids, solving the viral equivalent to Levinthal's Paradox in protein folding. Indeed, the PS code directs assembly towards a small number of efficient pathways within the vast complexity of combinatorially possible ones, hence giving the virus an advantage in the arms race against the host's immune defenses.

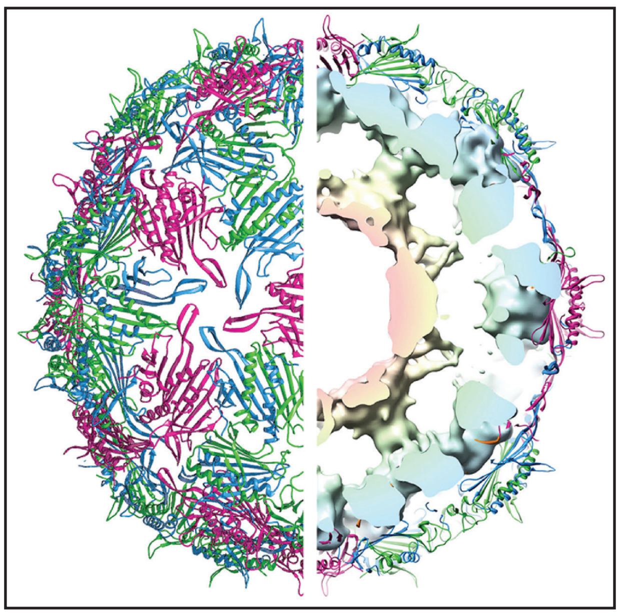

Figure 3. *The MS2 capsid is shown from the outside (left half), and as a cross-sectional view revealing ordered RNA density (right half) based on results in [5]. Our Hamiltonian path corresponds to the outer ring of RNA density in proximity to capsid. Image credit: Richard Bingham, adapted from a figure in [5] by James Geraets.*

Our modeling offered another astonishing conclusion. The impact of this construction manual can only be observed if capsid protein is ramped up slowly—as in the case of a real viral infection—rather than added in a single step, as is often the case in *in vitro* experiments. Inspired by this mathematical result, our collaborators at the University of Leeds performed assembly experiments under the condition of such a protein ramp, leading to the first direct experimental demonstration of PS-mediated assembly [8]. In collaboration with experimentalists at the University of Leeds—in particular my Wellcome Trust co-investigator Peter Stockley—and the University of Helsinki, we have since identified PSs in a number of human viruses and jointly hold a patent exploiting this discovery in anti-viral therapy.

A recent review by Peter Prevelige, a world-leading authority on virus assembly, is entitled "Follow the Yellow Brick Road: A Paradigm Shift in Virus Assembly" [9], in reference to our graph theoretical approach; we usually depict Hamiltonian paths in yellow (as in Figures 1 (on page 1) and 2 (left)). Ultimately, this research demonstrates that mathematics can drive discovery in molecular biology, functioning as a key player in interdisciplinary efforts to understand how viruses form, evolve, and infect their hosts.

This article is based on an invited lecture by Reidun Twarock at the SIAM Conference on the Life Sciences, which was held in Boston this July.

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Reidun Twarock is a professor of mathematical biology at the University of York. She has pioneered the area of mathematical virology, as well as the development of mathematical and computational techniques and models in an interdisciplinary context to address open problems in virus structure, assembly, and evolution.

Beating in Fluid: Hearts and Cilia by the Immersed Boundary Method

By Debbie Sniderman

Heart valves are thin flexible membranes immersed in fluid that profoundly affect blood flow. Each side of the heart uses valves to aid in the movement of blood from the atrium to the ventricle, and from the ventricle to the aorta or the pulmonary artery. Each ventricle has an inflow and an outflow valve, which allow the alternate contraction and relaxation of that ventricle to generate unidirectional flow. The valves open and close in coordination with the pumping of the heart in its two main states, the diastolic or relaxed phase and the systolic or contracted phase (see Figure 1). Heart valves let flow through when open, but the valve leaflets also shear the flow and create vortices that help the valves close efficiently. When closed, the valves prevent backflow.

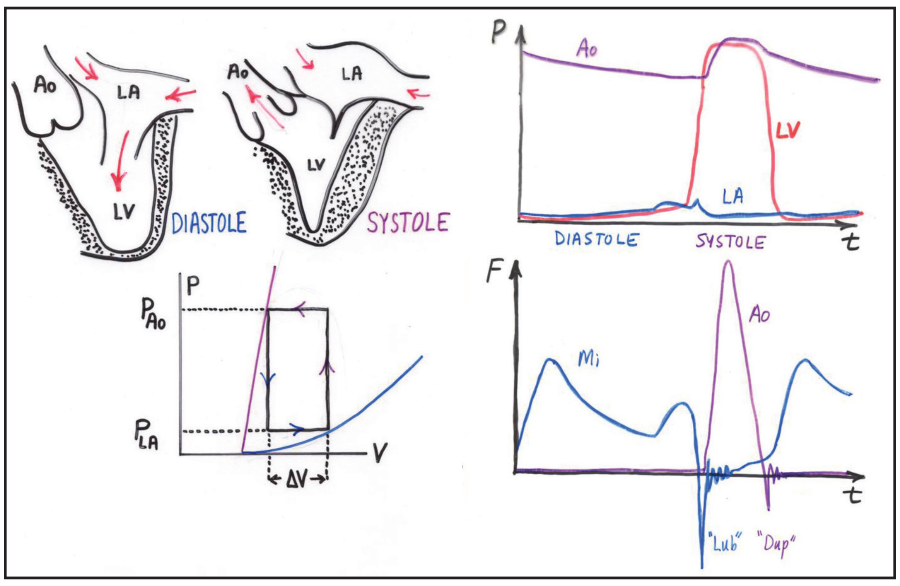

Figure 1. *Diagram showing the physiology of the left side of the heart. The right heart is qualitatively the same but quantitatively different.* **Upper left.** *Heart in its two main states, diastole (relaxed) and systole (contracted). LA=left atrium, LV=left ventricle, Ao=aorta.* **Bottom left.** *Pressure/volume diagram of the cardiac cycle. Each corner of the rectangular path denotes the opening or closing of a valve. Inflow and outflow pressures are idealized as constant. ΔV denotes the stroke volume.* **Upper right.** *Pressures in the Ao, LV, and LA. The ventricle switches between atrial pressure when relaxed and aortic pressure when contracted.* **Bottom right.** *Flows through the Ao and mitral (Mi) valves, with the heart sounds indicated. Image credit: Charles Peskin.*

Heart valve function presents a fluid-structure interaction problem, and the immersed boundary (IB) method offers a solution. It unifies the fields of elasticity and fluid dynamics, enabling a wide variety of applications in biological and engineering mechanics. Charles Peskin (New York University) first introduced the IB method in his Ph.D. thesis at the Albert Einstein College of Medicine, and further developed it with his students and colleagues at New York University's Courant Institute of Mathematical Sciences.

IB Method

The IB method [8] treats immersed elastic bodies or boundaries as a part of the fluid in which they are immersed. Structures are represented as elastic, and material points of the structure are tracked so that their spatial configurations can be used to compute elastic forces applied to the fluid. Fluid velocity and pressure are computed on fixed Cartesian grids.

The moving structure grid and the fixed fluid grid do not conform to each other, so the IB method's key problems are the following: determining how to apply the forces generated by the structure to the fluid and deciding how to evaluate the fluid velocity at the structure points. Use of a smoothed approximation to the Dirac delta function, constructed so that important physical quantities such as momentum and angular momentum are preserved during fluid-structure interaction, solves both of these problems. A recently-developed delta function with a constant second moment and three continuous derivatives enables a new version of the IB method, in which the interpolated velocity field is exactly divergence-free.

The principal advantage of the IB method over other methods for fluid-structure interaction is that there is no need to adapt the fluid mesh to that of the structure, or vice versa. There is also no need to deal separately with the many ways that the structure mesh may intersect with the fluid mesh.

The IB method is modular; it separates the task of modeling the fluid from that of modeling the immersed structure. Any structural model that can generate elastic forces from the spatial configuration of the structure mesh's nodes can be used. Peskin used networks of points connected by springs for structural models in his early work. More recently, finite element structural models are being immersed in fluid by the IB method. Since there is fluid everywhere in an IB computation, even inside an immersed structure, the structural model

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Biofluids of Reproduction

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connected by springs or Maxwell elements that transmit forces.

The group first looked at the rheology of viscoelastic structures in fluid to characterize the structures' properties when forces and shear are applied as single or periodic pulses. Then they introduced a flagellum with specified kinematics and particular waveform into the network (see Figure 2). The waveform makes it through the mesh without feedback from it, and deforms the compliant network. As flagella encounter denser networks they still pass through, but with lower velocities than in free space for most of the journey; however, a velocity boost is visible as the flagella exit the object. Even though the stored elastic energy in the network increases the velocity, the flagella require more power to maintain their waveforms in the denser environment, so their efficiency is seen to be less than in free Stokes flow.

Though there is still much analysis to be done, thus far the models reveal that a viscoelastic network can enhance swimming. Future models will include two-way coupling and won't prescribe the kinematics, preventing sperm from swimming with fixed amplitudes. As motors face more resistance, lower amplitude waveforms may result.

Encountering a "Wall"

Using an elastic model of a flagellum, Fauci's group also studies the elastic connections and binding proteins that attach sperm to an oviductal epithelial "wall." Shapes evolve based on other forces, and simulations help the researchers determine if the hyperactivated form allows flagella to more easily escape when attached to a wall.

As sperm approach a wall, elastic connections are created with forces able to attach it (see Figure 3). Simulations help visualize this interplay under different scenarios. With no elastic linkages, sperm get close to the wall but don't attach. With no-slip boundary conditions, they don't escape. When sperm enter hyperactived mode, they attach, detach, and reattach, consistent with experimental observations.

These simulations demonstrate that bond behavior can enable sperm movement away from an epithelial cell, and suggest the necessity of more experiments for further bonding characterization. Fauci's group also developed a system to simulate sperm's encounter with a network surrounding a solid sphere, and plans to study actual penetration mechanisms in more detail.

Going Hyperactive

Using mechanical forces, sperm can push themselves through viscoelastic networks to penetrate an egg. During symmetric flagellar bending, they take on linear trajectories and are surrounded by a resting level of calcium ions. Sperm swim straight; the moderate-amplitude beating of their tails has the quintessential sinusoidal wave form, with increasing amplitude towards the tail.

When activated by high levels of calcium, sperm enter a hyperactive state with a different motility pattern characterized by repeated, high-amplitude asymmetric beating. Sperm in this state move in circles and appear 'confused.' Hyperactivity is an important process that provides the higher mechanical forces necessary to unstick sperm from mucosal folds in the oviduct and prevent reattachment. These higher forces also allow sperm to penetrate the viscoelastic layer surrounding the ovum right before fertilization. Clear biochemical pathways initiate this state.

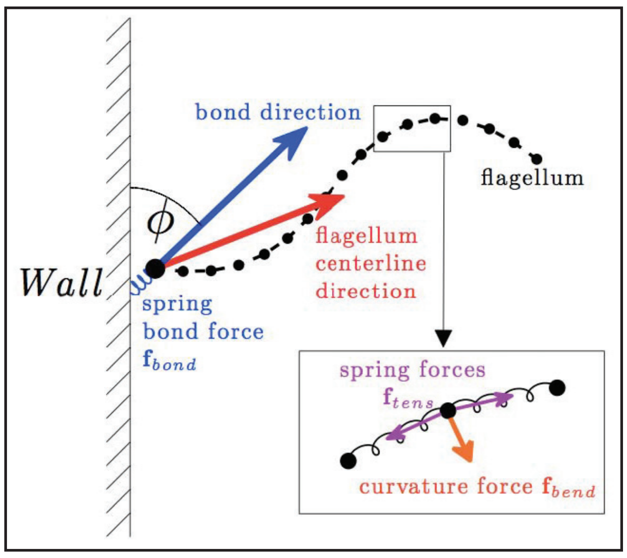

Figure 3. *Model of flagellar adhesion to a planar wall. Image credit: [1].*

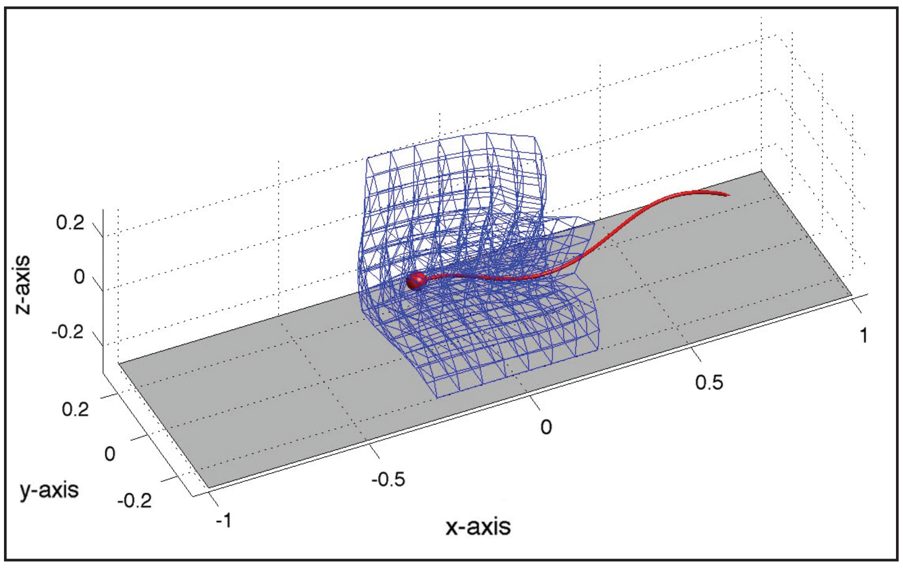

Figure 2. *Swimmer affects compliant viscoelastic network. Image credit: [2]. To view a simulation, visit the online version of the article at sinews.siam.org.*

Studying the mechanics, forces, and calcium dependence helps elucidate the functional implications of the hyperactivated mode of motility, and begs the following questions:

- What biochemical pathways initiate hyperactivation?
- What happens to sperm when exposed to sufficient calcium?
- What force-generating mechanisms change the beat?
- Compared to the force of moderate amplitude beating, how much more force does asymmetric bending generate to prevent the flagellum from sticking?

Biochemically-Activated Penetration

Sperm can also penetrate an egg by dissolving the network in front of it. When ready to fertilize the egg, a sperm cell's body releases enzymes that dissolve some of the links in the viscoelastic mesh.

Motivated by this occurrence, Fauci's group is currently working on computational experiments—applying forces and dissolving links—with these viscoelastic webs. They are attempting to couple the biochemical part of the puzzle with different reduced models of sperm motility. The group plans to study the penetration process in more detail to understand the significance of sperm-egg penetration mechanics in relation to its biochemistry and the interplay between the two.

This article is based on Lisa Fauci's AWM-SIAM Sonia Kovalevsky Lecture at the SIAM Annual Meeting, which was held in Boston this July.

View a photo of Fauci accepting her Kovalevsky Lecture prize on page 8.

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Hearts and Cilia

Continued from page 4

does not need to enforce incompressibility, a task that is handled by the fluid solver [1].

Immersed boundary software known as IBAMR, which was created by Boyce Griffith (University of North Carolina at Chapel Hill) and is publically available, incorporates both distributed parallelization and adaptive mesh refinement of Cartesian grids [2].

Beating Hearts

Peskin's work on the heart began with the goal of improving the design of artificial valves; for recent work of this kind, see [3]. The next step, carried out jointly with David McQueen (New York University), was to build a model heart around the valves [5, 6].

Heart muscle is made of fibers that take geodesic paths on nested toroidal surfaces within the heart walls. Peskin introduced equations for this fiber architecture [7] and found asymptotic solutions in the special case of axial symmetry (applicable to the left ventricle). But solving these equations in the non-axial symmetric case of the whole heart remains an open problem.

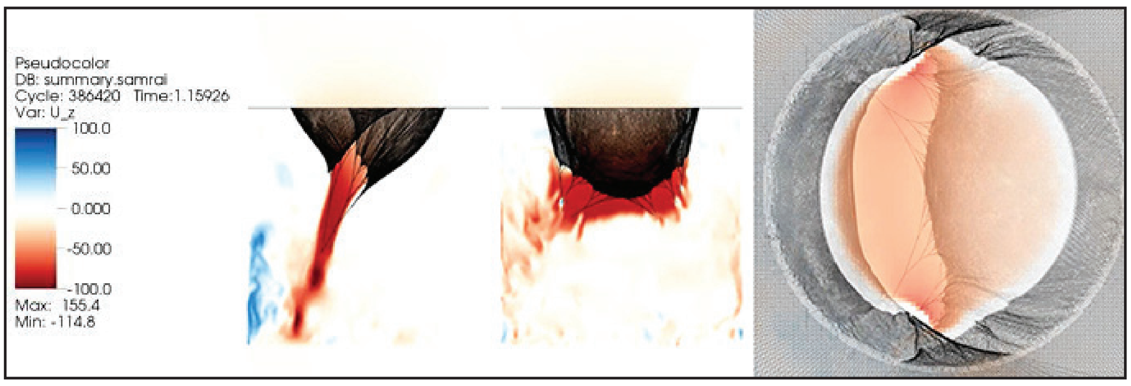

Figure 2. *Mitral valve model. Three perpendicular views of a mitral valve model simulated in a test chamber by the IB method. Colors indicate the vertical component of fluid velocity. Image credit: Alexander Kaiser. To view a simulation, visit the online version of the article at sinews.siam.org.*

Numerical solutions by McQueen and Peskin [9] of similar equations for the collagen fiber architecture of the aortic valve reveal a fractal structure with dimension 2.2 [10]. Alexander Kaiser (New York University) recently created a fiber-based model of the mitral valve with intricate chordae tendineae. In the IB model heart, all mathematical fibers are immersed or embedded in a viscous and incompressible fluid, creating a fiber-reinforced fluid that has mass, volume, and incompressibility. The stress/strain relationship of the muscle fibers is both nonlinear and time-dependent, with much higher stiffness during systole, or contraction of the heart, than diastole, the relaxation phase. This time dependence of material properties drives the model heart through the cardiac cycle (see Figures 2 and 3).

Beyond Mechanics and Fluids: Electrical Integration

The IB method's flexibility also allows for the integration of the electrical component of the heart [4] into the mechanical component/fluid modeling. The heart has an autonomous system that generates electrical waves to control beating. Mechanical-to-electrical feedback operates through stretch-activated channels and passive changes in electrical resistance as cardiac tissue deforms during contraction and relaxation.

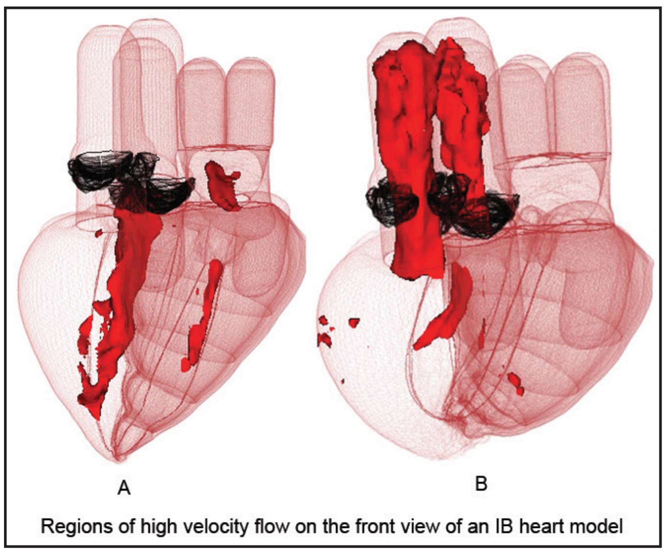

Figure 3. *Snapshot of a visualization of regions of high velocity flow on the front view of an IB heart model stimulated by electrical activity. The red color indicates regions in which the magnitude of the velocity is above an arbitrarily chosen threshold. A is in diastole with blood entering the ventricles through the mitral and tricuspid valves. B is in systole, with blood being ejected from the ventricles through the aortic and pulmonic valves. In both frames the thin-walled right ventricle is on the left side of the figure. Image credit: Boyce Griffith, David McQueen, and Charles Peskin. To view a simulation, visit the online version of the article at sinews.siam.org.*

In joint work with Griffith, Peskin uses the formalism of the IB method to simulate the electrical and mechanical activity of the heart within the same framework and in the same software. Their work is based on the bidomain model, which tracks both intracellular and extracellular voltage and current. In the IB formulation of the bidomain equations, the extracellular domain is analogous to the fluid and the intracellular domain is analogous to the structure.

In the electrical equations of the extracellular and intracellular spaces, the currents leaving the cells appear as a source/sink term. This can be written mathematically as a distributed delta function, which spreads the current onto the extracellular domain identically to how forces are applied to fluid in the IB method. The transmembrane current depends on both intracellular and extracellular voltage, and the evaluation of the extracellular voltage at a given intracellular point is analogous to the evaluation of fluid velocity at a structure point in the IB method. Thus, the entire electrical problem looks like an IB problem.

In the IB formulation, the extracellular space extends beyond the myocardium and into the blood and surrounding tissues, both of which are electrically conducting media. The model heart thus acquires an electrocardiogram.

Beating Cilia

Another example of beating in fluid on a microscopic scale occurs in motile cilia, which are the active hair-like appendages of biological cells. The beat of a single cilium is driven by hundreds of dynein molecular motors that coordinate their activity to produce wavelike bending of the cilium.

In a model proposed recently by Peskin and Jihun Han (New York University), the coordination emerges spontaneously as a result of a simple dynamical law governing the tension of each dynein motor, together with a geometrical constraint based on the microstructure of the cilium. The IB method immerses the model cilia in fluid, facilitating the study of their fluid-mediated interaction (see Figure 4). These studies reveal a striking tendency towards synchronization of nearby cilia regardless of initial conditions.

The mathematical problems surrounding hearts and cilia are so different in scale, yet both involve spontaneous oscillation and fluid-structure interaction. The immersed boundary method is applicable to both.

This article is based on an invited lecture by Charles Peskin at the SIAM Conference on the Life Sciences, which was held in Boston this July.

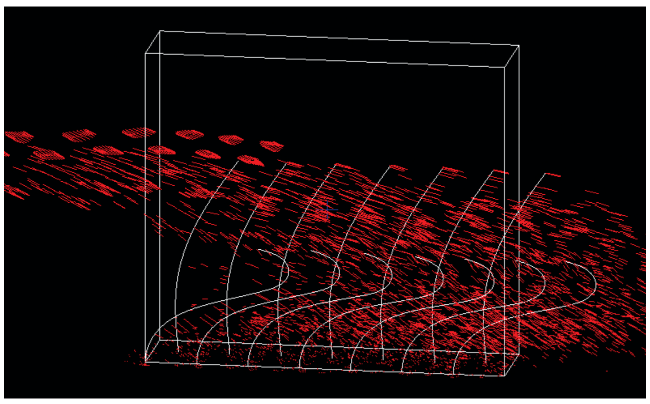

Figure 4. *Snapshot of two rows of modeled cilia in a periodic box of fluid. Red particles are fluid markers leaving trails to show recent trajectories. Despite in-phase initial conditions, the two rows temporarily go into anti-phase and later recover synchrony before computations end. Long-term behavior is unknown. The more vertical cilia are moving left (power stroke) and the others are moving right (recovery stroke). Image credit: Jihun Han. To view a simulation, visit the online version of the article at sinews.siam.org.*

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Careers Outside Academia: How Should Math and Applied Math Students Prepare?

By Lalitha Venkataramanan, Rachel Levy, and Bill Kolata

Graduate students often look to their thesis advisors as their main mentors. Hence, many students want to continue in academia. Recent data analysis by Bill Kolata[1] indicates that the number of graduating students is much larger than can be absorbed by the academic community. The total number of mathematics Ph.D.s awarded in 2013-2014 was approximately 1,187. On the other hand, the number of tenure track positions in math departments filled by students with a Ph.D. was 187 (38 in doctoral-granting institutions). 556 doctoral graduates (44.6%) accepted postdoctoral positions. The 2012 SIAM Mathematics in Industry Report[2] suggests that "University faculty must actively encourage students to consider careers in industry and prepare those students for the very different world they will encounter upon graduation." The 2015 NSF-IPAM Mathematical Sciences Internship Workshop Report[3] echoes this proposition and discusses recommendations for infrastructure and programs that could increase the number of internships targeting mathematical sciences students. With this in mind, SIAM hosted a panel discussion on careers in industry at the 2016 SIAM Annual Meeting, held in Boston this July. The panel was organized by the authors of this article.

Panelists Tamara Kolda (Sandia National Laboratories), Dean Bottino (Takeda Pharmaceuticals), Gary Green (The Aerospace Corporation), Penny Anderson (MathWorks), and Amy Sliva (Charles River Analytics) discussed their journeys from graduate school to their current jobs and fielded questions from the audience. The panel touched on a few themes, which are highlighted below.


From left to right: Penny Anderson, Dean Bottino, Amy Sliva, and Gary Green field questions from the audience during a panel discussion on careers in industry at the 2016 SIAM Annual Meeting. SIAM photo.

How should students prepare for a career in industry?

The panelists urged undergraduate, graduate, and postdoctoral students to take computer science courses. In particular, achieving programming proficiency in C, Python, or MATLAB is very valuable in demonstrating and testing the feasibility of a research method. Since mathematicians are often involved in data science, the panelists also recommended that students take sufficient statistics courses to enable data modeling. In addition, industrial internships during the summer months of the first few years of graduate school offer students a glimpse into what is required for an industrial career.

What do companies look for during the interview process?

Interviewers at companies look, first and foremost, for relevant technical experience. Equally important is demonstration of mathematical maturity: the ability to look beyond the underlying problem, perceive the big picture, and question the problem formulation if necessary. Moving from one problem to another is often a challenge for students who have spent many years working on the same problem in graduate school. This flexibility in transitioning between different problems is an important component of working in industry. In addition, most industrial mathematicians work on a team with other scientists and engineers. Thus, it is important to learn to communicate well within a team and be a team player. Finally, mathematicians are often asked to explain their work to upper management who may not have the same mathematical background. A short "elevator pitch" targeted towards a specific stakeholder should be relevant and capable of explaining the work in sufficient detail to capture its value.

What would you recommend to a student who is getting their bachelor's degree in math or applied math and is interested in an industry job?

To make yourself easily marketable, try to pick up a second degree with a major in a complementary subject, such as computer science or a relevant science. Some companies offer programs to mentor young mathematicians that allow them to keep their jobs while pursuing a master's degree or a Ph.D. If applicable, discussing this option during the interview process is useful.

How difficult is it to give up teaching?

Moving from academia to industry means giving up teaching, and this can be quite challenging. However, the ability to make a difference in the workplace can often replace the joy of teaching. Technical guidance of company interns can have a similar feel to academic teaching. In addition, mentoring junior scientists at the workplace can be quite rewarding. Mentoring can be done formally (through a program at a company or through association with a society, such as the Association for Women in Science) or informally (meeting periodically with a junior colleague).


From left to right: Tamara Kolda and Penny Anderson discuss their paths to industrial careers during a panel disucssion at the 2016 SIAM Annual Meeting. SIAM photo.

How is work evaluated at your company?

In academia, a faculty member's work is evaluated based on his or her teaching and research abilities. In industrial research, technical work is also evaluated on the quality of applied research. Some aspects of this research may be written in peer-reviewed publications or presented at conferences. However, the technical work is more often captured in invention disclosures, which is the first step towards a patent. Technical work also frequently results in some features of software code that can be used internally within a company or commercialized and shared outside. Experience with business strategy, mentoring and community leadership, and professional visibility at conferences and universities are other benchmarks used to evaluate a scientist/engineer's performance.

Lalitha Venkataramanan is a scientific advisor in the Mathematics and Modeling Department at Schlumberger-Doll Research, Cambridge. She is a member of the SIAM Industry Committee, the Society of Petroleum Engineers, and the Society of Petrophysicists and Well Log Analysts. Rachel Levy is SIAM VP for Education, as well as an associate professor in the Department of Mathematics and Associate Dean for Faculty Development at Harvey Mudd College. Bill Kolata is the technical director of SIAM.

Tamara Kolda

Career trajectory:

- Ph.D. in applied mathematics from the University of Maryland
- Postdoctoral fellowship at Oak Ridge National Laboratory
- Currently a Distinguished Member of Technical Staff at Sandia National Laboratories in Livermore, CA

Research interests: Multilinear algebra and tensor decompositions, graph models and algorithms, data mining, optimization, nonlinear solvers, parallel computing, and the design of scientific software

Works with: Electrical, chemical, and mechanical engineers, computer scientists, and statisticians

Fun fact: Teaches yoga

Dean Bottino

Career trajectory:

- Ph.D. in mathematical biology from Tulane University
- Postdoctoral fellowship from the University of Utah, and National Institutes of Health (NIH) postdoctoral fellowship at the University of California, Berkeley
- Joined Physiome Sciences and eventually Novartis as associate director and oncology modeling and simulation group lead; later led the modeling and simulation oncology group at Roche Pharmaceuticals
- Led a team for clinical translational modeling and simulation at Millennium Pharmaceuticals (now Takeda)

Research interests: Mathematical biology, oncology modeling, and simulation for better decision-making

Works with: Clinical pharmacologists, biomarker experts, physician-scientists, and biostatisticians

Fun fact: Was executive vice president of a two-person company, BioAnalytics Group LLC, before joining Novartis

Gary Green

Career trajectory:

- B.S. from the University of Idaho
- M.S. from Michigan State University
- Ph.D. from Pennsylvania State University
- Taught for many years in the California State University system
- Employed (since 1974) at The Aerospace Corporation, a nonprofit company that works primarily in national security space

Research interests: Problems related to launch vehicle simulation and development, satellite visibility and proximity, space system performance, satellite-based navigation and geolocation, and space system threat analysis

Works with: A variety of people with degrees in the mathematical, engineering, and physical sciences, most of whom can be classified as systems engineers who, although grounded in a particular field of interest, are cognizant of the many disciplines required to build space systems

Fun fact: Conducts a STEM-driven mathematics enrichment program for elementary students, showing them that mathematics can be fun and exciting

Penny Anderson

Career trajectory:

- B.S. in mathematics from McGill University
- M.S. in computer science from McGill University
- Senior Engineering Manager at MathWorks

Research interests: Numerical analysis and mathematical software development

Works with: Software engineers, marketing staff, quality engineers, documentation and user experience personnel

Fun fact: Currently works in the Boston suburbs, a long way from sunny Barbados where she grew up

Amy Sliva

Career trajectory:

- Ph.D. from the University of Maryland, where she developed probabilistic models to simulate complex systems
- Tenure track professor at Northeastern University
- Involved in building intelligent systems at Charles River Analytics

Research interests: Building intelligent systems, forecasting and predictive modeling, and data science

Works with: Computer scientists, cognitive scientists, psychologists, and applied mathematicians

Fun fact: Loves the interplay between computer and political science; has a double major in both and a masters in international security and economic policy

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[1] http://www.ams.org/profession/data/annual-survey/2014Survey-RecruitmentHiring-Supp-TableR1.pdf

[2] http://www.siam.org/reports/mii/2012/report.php

[3] http://www.ipam.ucla.edu/reports/2015-nsf-ipam-mathematical-sciences-internship-workshop-report/

High-Performance Computing for the Detection of Strokes

By Victorita Dolean

Cerebrovascular accidents (CVAs) or strokes are caused by a perturbation in the blood supply of the brain, leading to a quick loss of cerebral functions that is very often lethal. There are two categories of CVAs: ischemic strokes (80% of cases), resulting from the occlusion of a cerebral artery, and hemorrhagic strokes (20% of cases), provoked by a bleeding vessel. From a medical point of view, the detection and characterization of CVAs are crucial for patient survival.

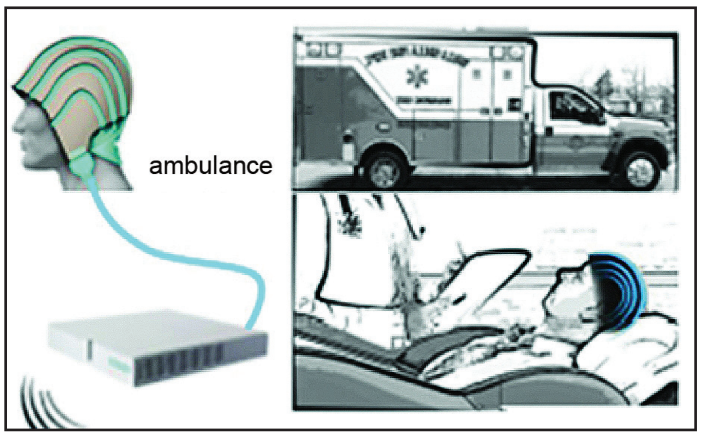

Figure 1. *Principle of microwave imaging. Image courtesy of EMTensor.*

Continuous monitoring of the brain requires an image taken every fifteen minutes. Nowadays physicians use two imaging systems of the brain: magnetic resonance imaging (MRI) and cerebral tomogram (CT) scans. Even when these techniques are very precise, their use is not well adapted to efficient medical care. Moreover, they can be harmful, as in the case of continuous monitoring with CT scans that measure X-ray absorption by tissues.

Our research team, which won the Bull-Joseph Fourier Prize in 2015,[1] carried out its work in collaboration with EMTensor,[2] an Austrian innovative SME dedicated to biomedical imaging. For the first time ever, we have demonstrated on synthetic data the feasibility of a new imaging technique based on microwaves (see Figure 1). This technique allows for the characterization of CVAs, beginning with the very first instance of patient care in an ambulance and extending to continuous patient monitoring during hospitalization.

How does it work? Electric properties of biological tissues are a great indicator of the tissues' functional and pathological condition. Microwaves can image them, on the basis of differences in their dielectric properties. In such a system, a patient's head is equipped with a helmet consisting of electromagnetic antennas that transmit data to a high-performance computing (HPC) center, which sends images of the brain to doctors at the hospital where the patient will be treated. This type of imaging requires a reduced data acquisition phase with a satisfying spatial resolution; it is less harmful than using a mobile phone. These characteristics make microwave imaging very appealing. From a computational point of view, microwave imaging solves an inverse problem and subsequently a fast solution of Maxwell equations. To prove the feasibility of such a technique, we have developed a HPC approach that generates brain images in less than 15 minutes.

In order to develop a robust and precise methodology for microwave imaging, one must master a few distinct research fields: optimization, inverse problems, approximation, and solution methods for the simulation of the direct problem modeled by Maxwell equations. The precise simulation of a direct problem for a complex and highly heterogeneous medium is a challenge in itself. We used a few tools previously developed by the team's researchers: the HPDDM[3] library for domain decomposition and its interface with the FreeFem++[4] software (finite elements).

EMTensor's experimental system to be simulated consists of an electromagnetic reverberating chamber surrounded by five layers of 32 antennas each, able to work alternately as emitters or receptors (see Figure 2). The object to be reconstructed is introduced in the chamber. Alternately, each of the 160 antennas emits a signal at a fixed frequency, typically 1 GHz. The electromagnetic field propagates into the chamber, which allows the correct reconstruction (what we call imaging) of its dielectric properties. The other 159 antennas record the total field in the form of complex transmission, and the inversion algorithm reconstructs a brain image on the basis of this data. Our first step involved successfully comparing the measure of data acquisition made with EMTensor's system with those numerically performed by the resolution of Maxwell equations on a 3D mesh.

In the next step, we created synthetic data on a brain model coming from scan sections (362x434x362 voxels) and then simulated a hemorrhagic CVA. Lastly, we designed and tested an inversion algorithm for monitoring the evolution of the CVA, reconstructed by successive slices. Here, a slice corresponds to one layer of 32 antennas equipping the experimental system. The use of parallelism allows the reconstruction of each layer to be generated independently, and the inversion algorithm uses 4,096 computing cores to

See **Strokes** *on page 8*

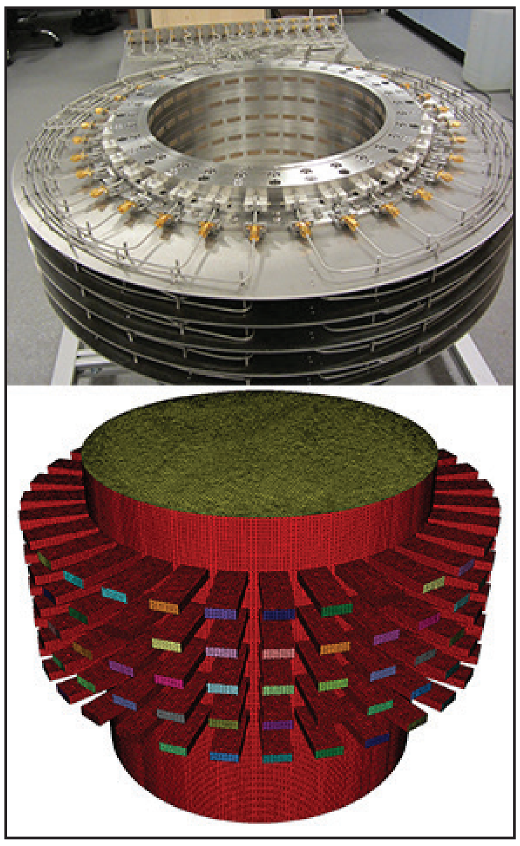

Figure 2. *Measurement chamber (above) and corresponding mesh (below) for numerical simulation (diameter: 28.5 cm). Image courtesy of EMTensor.*

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[1] http://atos.net/en-us/home/we-are/news/press-release/2016/pr-2016_04_12_02.html

[2] http://emtensor.com/

[3] https://github.com/hpddm/hpddm

[4] http://www.freefem.org/

Photos from the 2016 SIAM Annual Meeting

SIAM President Pam Cook (left) and AWM President-Elect Ami Radunskaya (right) present Lisa Fauci (Tulane University) with the AWM-SIAM Sonia Kovalevsky Lecture at the Prizes and Awards Luncheon during the SIAM Annual Meeting. Read more about her lecture on page 1. SIAM photo.

The 2016 SIAM Fellows were honored during the SIAM Business Meeting at the 2016 Annual Meeting. Bottom row, left to right: Clint N. Dawson (University of Texas at Austin); Michael C. Reed (Duke University); Helena J. Nussenzveig Lopes (Universidade Federal do Rio de Janeiro); Françoise Tisseur (University of Manchester); Xiaoye Sherry Li (Lawrence Berkeley National Laboratory); Cynthia A. Phillips (Sandia National Laboratories); Sabine Van Huffel (KU Leuven). Top row, left to right: Xiao-Chuan Cai (University of Colorado Boulder); Gang Bao (Zheijiang University); Chandrajit Bajaj (University of Texas at Austin); Paul C. Bressloff (University of Utah); Michael Hintermüller (Weierstrass Institute for Applied Analysis and Stochastics and Humboldt-Universität zu Berlin); Bo Kågström (Umeå University); Alan J. Laub (University of California, Los Angeles); James G. Nagy (Emory University); Andrew Knyazev (Mitsubishi Electric Research Laboratories and professor emeritus at the University of Colorado Denver); David P. Williamson (Cornell University). SIAM photo.

Donald E. Knuth (Stanford University) receives the John von Neumann Lecture at the Prizes and Awards Luncheon during the SIAM Annual Meeting. Here he stands with SIAM President Pam Cook (left) and SIAM Executive Director Jim Crowley (right). SIAM photo.

SIAM President Pam Cook (left) poses with Tadashi Tokieda (University of Cambridge and Stanford University), who gave the I.E. Block Community Lecture at the 2016 SIAM Annual Meeting. Read more about his lecture on page 12. SIAM photo.

SIAM President Pam Cook (left) awards Linda Petzold (University of California, Santa Barbara) with the SIAM Prize for Distinguished Service to the Profession at the Prizes and Awards Luncheon during the 2016 SIAM Annual Meeting. SIAM photo.

Strokes

Continued from page 7

reconstruct an image in less than two minutes (94 seconds). Figure 3 depicts this reconstruction. The restitution time, which can be further refined, already fits the physicians' objective to receive an image every fifteen minutes to efficiently monitor the patient.

The medical and industrial challenge of this work cannot be emphasized enough. It is the first time that such a realistic study has demonstrated the feasibility of microwave imaging. Although the technique is less precise than MRI or CT scans, its low price, reduced size, and lack of adverse effects even with continuous use could make microwave imaging of the brain the equivalent of echography (ultrasound imaging) on other parts of the human body.

More details can be found in the preprint "Microwave Tomographic Imaging of Cerebrovascular Accidents by Using High-Performance Computing," http://arxiv.org/abs/1607.02573.

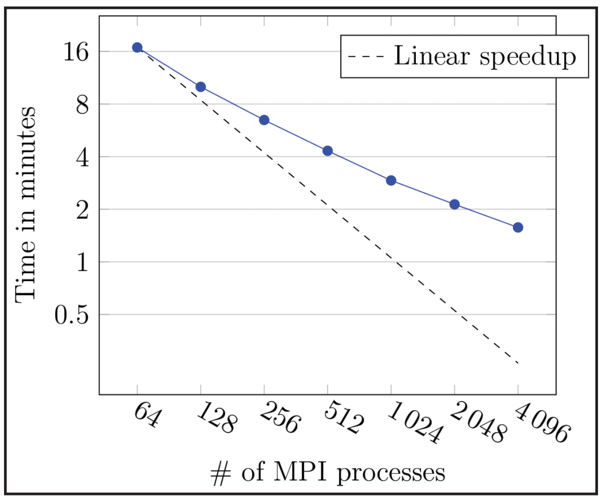

Figure 3. *Reconstruction time of an image regarding the number of computing cores. Mesh of the computational domain was generated by FreeFem++, software developed by Dolean's research group.*

Acknowledgments

This work has been supported in part by ANR[5] through the project MEDIMAX (led by C. Pichot from LEAT[6] of the University of Nice). Large-scale numerical simulations have been possible thanks to the technical support and computing hours on large supercomputers: Curie (CEA, Bull) and Turing (CNRS, IBM) via GENCI[7] (allocations 2016-067519 and 2016-067730) or PRACE[8] calls.

Collaborators on HPC: F. Hecht, F. Nataf, P.H. Tournier (University Pierre and Marie Curie University, France), and P. Jolivet (University of Toulouse, France).

Victorita Dolean is currently a reader in the Department of Mathematics and Statistics at the University of Strathclyde, Glasgow, United Kingdom. She has co-authored around 50 research papers and conference proceedings and is part of the team that received the 2015 Bull-Joseph Fourier Prize, awarded yearly in France for important algorithmic advances in high performance computing.

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[5] French National Research Agency

[6] http://leat.unice.fr/

[7] http://www.genci.fr/en

[8] http://www.prace-ri.eu/

Computational Behavioral Ecology
New Insights into Animal Social Behavior

By Debbie Sniderman

Behavioral ecologists study ecological and evolutionary aspects of animal behavior and their adaptation to surrounding environments. Traditionally, they had to visit the field, take notes, and make observations when gathering behavioral data. This was a sparse form of observation wrought with limitations. Today, an abundance of data about wild populations is available in scales that are orders of magnitude richer than before, thanks to photos, videos, sensors, and new collection technologies such as GPS, high-definition cameras, unmanned aerial vehicles (UAVs), genotyping, and crowdsourcing. Computational investigation of this data is fundamentally changing the way biologists study nature through analysis, hypothesis formation, and visualization of complex data sets.

The computational work of Tanya Berger-Wolf (University of Illinois at Chicago) has facilitated the scientific process of understanding animal sociality at individual, group, and interaction levels in the context of animals' own environments.

"Even the questions being asked are changing because of the data," Berger-Wolf says. "Visualizations need to change to provide answers that aren't only in terms of text, but also appeal to the visual ways through which humans process information in an immersive dynamic environment where an analysis can be overlaid into a virtual world, such as a construction of an African Savannah with individual animals moving around it."

Answering New Questions

Berger-Wolf is pioneering the analysis of high-resolution data for behavioral scientists, who have struggled with its use over the last decade. Computational techniques are exploratory and offer predictive models and tools to explain why animals are social and how they move. Such techniques also offer insights about how to find and identify key individuals in a group, how the group makes decisions, and whom it decides to follow. Computational pattern recognition techniques identify specific animals with unique markings, helping answer questions about population dynamics and ranges.

Berger-Wolf uses data from a wide variety of sources to provide scientific insight into collective behavior of animals such as zebras, baboons, and humans. Analyzing animal trajectories and movement patterns allows her group to identify long-term affiliates, group leaders, and individuals that initiate changes, i.e. from browsing to moving in coordinated groups.

Behavioral ecologists use video cameras to track Quick Response (QR) or color-coded insects and small animals such as ants and frogs with fluorescent numbers. Larger animals wear GPS collars with solar batteries, which identify location and inferred proximity within a network. Computer vision provides even more detailed information about the direction in which animals are looking. In the future, tiny radio antennas may help observe bird and insect migration.[1]

Remotely-sensed data can count populations, enable conservation, locate or assist highly endangered species, and identify survival rates of a group or species. But locating animals is not enough when studying behavior; researchers need to know which specific animals have been located. For instance, location data from a GPS can show an animal leading a group, but it doesn't provide information about its age, gender, or rank in the population. That type of tracking requires image data.

Animal signatures such as stripes, spots, notches, or wrinkles are unique and easily identifiable from any angle through image data. Berger-Wolf and her colleagues have developed an algorithm (HotSpotter) for automatically recognizing individual animals from images using these visual signatures, and built an Image-Based Ecological Information System (IBEIS) that allows tracking of individuals and populations using this data. The identification algorithm uses algebraic scale-invariant feature transform (SIFT) features to find key pixels in images that are invariant to photo angles and scales. It then matches those pixels in different images to determine whether it is the same individual.

Inferring Behavior from Remote Sensing

Margaret Crofoot (University of California, Davis), a collaborator of Berger-Wolf, tracked entire baboon troops for 30 days using GPS collars at one-second intervals. International Space Station (ISS) receiver transmitters then collected location data, animal position, animals in close proximity, and orientations, creating new GPS data that didn't previously exist for baboons or other animal populations.

Using data from the 30-day observations,

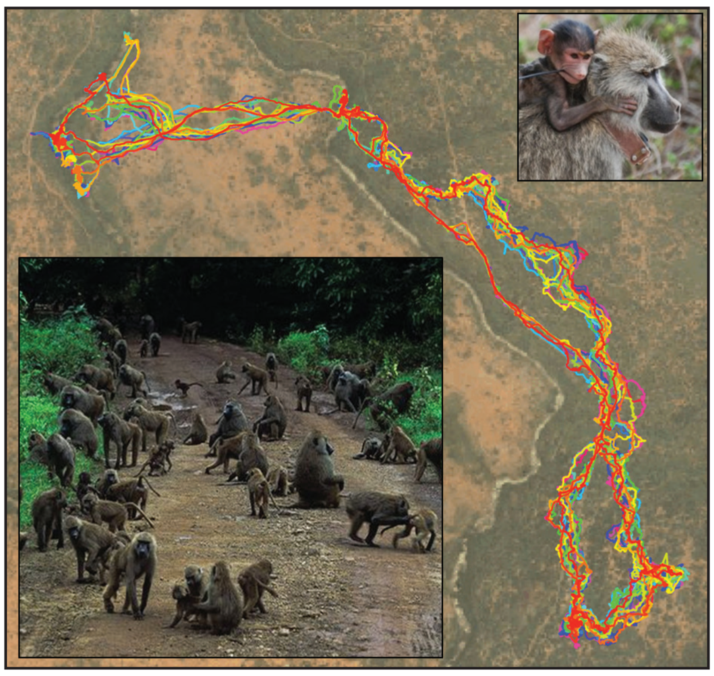

Figure 1. *Trajectories of locations of individuals in social animal networks can help researchers understand decision processes and test whether the network can predict behavior. Berger-Wolf found that both nearest neighbors and long-term affiliates predict individual locations during collective movement in wild baboons. Image credit: [1].*

See **Behavioral Ecology** *on page 11*

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[1] http://icarusinitiative.org/

Stanley Osher Receives the William Benter Prize in Applied Mathematics

Stanley Osher

City University of Hong Kong (CityU) has awarded the William Benter Prize in Applied Mathematics 2016 to Stanley Osher of the Department of Mathematics at the University of California, Los Angeles (UCLA), for his significant contribution in developing and applying mathematics to solve real-world problems.

Osher is one of the most influential and active computational and applied mathematicians of our time. His seminal and fundamental contributions in developing mathematical methods and efficient algorithms, such as shock capturing schemes, level set methods, the Total Variation model and Bregman algorithms, have revolutionised many fields, ranging from computational fluid dynamics and multiphase problems to optimisation and image processing.

The William Benter Prize in Applied Mathematics was set up in 2010 by the Liu Bie Ju Centre for Mathematical Sciences at CityU in honour of Mr William Benter, the donor of the prize, for his dedication to, and generous support for, the enhancement of the University's strength in mathematics. The Prize recognises outstanding mathematical contributions that have had a direct and fundamental impact on scientific, business, finance and engineering applications. It includes a cash prize of US$100,000 and is given once every two years.

The Prize was presented to Stanley Osher at the opening ceremony of the International Conference on Applied Mathematics, organised by the Liu Bie Ju Centre for Mathematical Sciences at CityU on 30 May 2016.

Biographical Sketch

Stanley Osher was born in 1942 in New York, USA. He obtained his Bachelor of Science in 1962 from Brooklyn College, and his Master's (1964) and PhD (1966) from New York University. He has been a Professor of Mathematics at the University of California (Los Angeles) since 1977. Before he joined UCLA, he was Professor of Mathematics at SUNY, Stony Brook University in New York, USA.

Osher has received many awards and honours for his achievements and contributions over the years. He is a Member of the US National Academy of Sciences and the American Academy of Arts and Sciences. He received the Carl Friedrich Gauss Prize 2014 at the International Congress of Mathematicians (ICM), the SIAM Kleinman Prize in 2005, and the Pioneer Prize at ICIAM 2003. He was a plenary speaker at the ICM in 2010 and gave the SIAM John von Neumann lecture in 2013. He is one of the most highly cited researchers in both mathematics and computer science in the world, and over 200 of his papers listed in the ISI (Web of Science) have been collectively cited more than 24,000 times.

Citation

The methods invented or co-invented by Stanley Osher have spread far beyond the traditional numerical analysis and computational mathematics community.

Osher and his collaborators have made fundamental contributions in designing a class of simple and efficient numerical schemes that can capture discontinuities in solutions with high-order accuracy and stability. The most significant of these are the ENO (essentially non-oscillatory) scheme and WENO (weighted ENO) scheme, which have been extremely successful in applications such as aero and fluid dynamics, airplane design, computer vision and image processing.

Another major area of Osher's research is the level set method, co-invented with James Sethian, which has revolutionised the handling of complicated interface geometry, dynamics and topological change on fixed grids. Their work has been applied to areas ranging from image processing and movie animation to semiconductor chip design and criminal prosecution.

Osher's work with Rudin and Fatemi on the Total Variation model for image processing is one of the earliest and most influential work on PDE-based methods for image processing. Total Variation has also become the most popular and useful regularisation used in image processing, compressive sensing, medical imaging and inverse problems in general.

The Merriman-Bence-Osher scheme for diffusion generated motion by mean curvature helped found the field of threshold dynamics and has proven to be of great value in data classification, material science and elsewhere.

The most recent significant work of Osher is the development of a new class of very fast numerical methods for optimization problems. These are central to the new fields of compressive sensing, matrix completion, robust principal component analysis and related topics. This is one of the most important developments in current applied mathematics.

– City University of Hong Kong

Mathematical Molecular Bioscience and Biophysics

A Recurring Theme at the SIAM Conference on the Life Sciences

By Guo-Wei Wei

How effectively does a potential drug bind to its target biomolecule? Mathematics has the answer! The SIAM Conference on the Life Sciences (LS16), held in Boston this past July, has, for the first time in its history, highlighted mathematical molecular bioscience and biophysics (MMBB) as a theme. MMBB concerns the development of mathematical theories, models, methods, schemes, and algorithms for elucidating molecular mechanisms and for solving open problems at the forefront of molecular biosciences and biophysics, such as those associated with drug design and discovery. All areas of mathematics—including differential equations, functional analysis, harmonic analysis, Lie group, Lie algebra, geometry, graph theory, and topology—are essential to MMBB and play a key role in addressing fundamental challenges in molecular biosciences and biophysics. One of these challenges is the emergent complexity in self-organizing biomolecular systems, such as HIV or Zika virus, molecular motors, Alzheimer's disease, and cancer cells. Mathematical approaches, such as multiscale modeling, invariant manifold, compressed sensing, and machine learning techniques, are becoming increasingly popular in molecular biosciences due to their ability to efficiently reduce the number of degrees of freedom while still maintaining an essential and adequate description of the biomolecules of interest [1, 2].

An important trend in contemporary life sciences is the fundamental transition of traditional disciplines, such as physiology, population biology, evolutionary biology, neuroscience, etc., from macroscopic and phenomenological subjects to molecular-based biosciences. Parallel to this development, the life sciences in the 21st century are transforming from qualitative and descriptive disciplines to quantitative and predictive ones, which are based on molecular mechanisms (the ultimate truth of biological sciences). This transformation has led to the burgeoning of MMBB, an emergent field in mathematics that generates mathematically-driven advances in molecular biosciences.

LS16 featured nine MMBB minisymposia organized by leading researchers in MMBB, covering various exciting advances including charge transport, ion channels, membrane modeling and computation, multiscale modeling of solvation, electrostatics computing and applications, topological and geometric methods for biomolecules, and macromolecular structures and interactions. The achievements in mathematical approaches for drug design and discovery are particularly worth noting.

Designing efficient drugs for curing diseases is especially important for life sciences in this century. Indeed, one of the ultimate goals of molecular bioscience and biophysics is to understand the molecular mechanism of human diseases and to develop efficient drugs—free of side effects—for disease treatment. The principal task of drug design and discovery is to predict whether a given molecule will bind to a biomolecule, such as a protein or DNA, and activate or inhibit its function, which in turn results in a therapeutic benefit to the patient. Typical drugs are comprised of small organic molecules, but biopolymer and protein-based drugs are becoming increasingly common. An ideal drug should be acceptable to the human metabolic system and bind firmly to the target, without affecting any other important "off-target" molecules or antitargets similar to the target molecule. Nevertheless, drug design and discovery involve an extremely complicated procedure that includes the following: disease identification, target hypothesis (the activation or inhibition of drug targets), screening of potential drugs that can effectively bind to the target, optimization of the structures of identified drugs, preclinical *in vitro* and *in vivo* tests, clinical trials to determine bioavailability and therapeutic potential, and optimization of a drug's efficacy, toxicity, and pharmacokinetic properties.

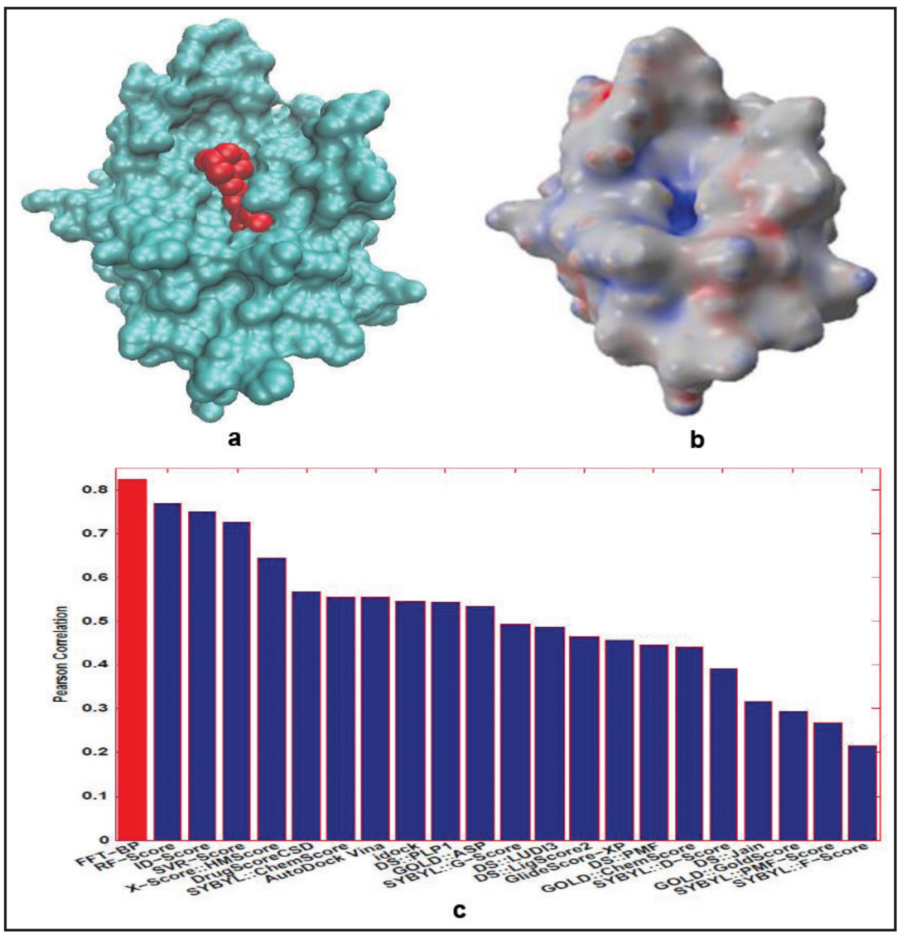

Figure 1. *Illustration of mathematical approaches to drug design and discovery.* **1a.** *Geometric representation of protein-ligand binding. The protein is green and the ligand is in red. Image credit: Kelin Xia.* **1b.** *The binding site (blue) predicted by the product of minimal curvature and electrostatic potential obtained from the differential geometry-based Poisson-Boltzmann equation. Image credit: Kelin Xia.* **1c.** *Comparison of Pearson correlations of various predictions and experimental binding affinity data for the PDBBind 2007 core set of 195 complexes. The winner, feature functional theory-binding predictor (FFT-BP), is based on machine learning and involves geometry, topology, graph theory, partial differential equations, and advanced numerical algorithms. Image credit: Bao Wang and Duc Nguyen.*

Computer-aided drug design and the design of protein containers for drug delivery have a proven record of success, not only because of improved understanding of the basic science—the molecular mechanism of drug and protein interactions—but also because of advances in mathematical modeling, geometric representations, topological characterization, graph theory analytics, computational methods, optimization procedures, machine learning algorithms, and the availability of massive parallel and graphics processing unit (GPU) computers. Indeed, mathematics plays an essential role in rational drug design, from the identification of drug-binding hot spots, consensus scoring, geometric analysis, cluster analysis, and global optimization to drug efficacy, toxicity, and pharmacokinetic analysis.

Moreover, mathematical approaches—such as geometric analysis for high throughput drug screening, persistent homology for protein-drug binding detection, reduced manifold representation for discriminating false protein-protein and protein-drug interfaces, and machine and manifold learning techniques for protein-drug binding site analysis—greatly impact drug design and discovery. Specifically, these approaches lead to better homology modeling, geometric models, molecular docking algorithms, molecular dynamics, quantum calculation, *de novo* design, and statistical models for efficient drugs and functional proteins. Figure 1 illustrates the Pearson correlations between experimental protein-ligand binding affinities and various theoretical predictions. A mathematical approach called feature functional theory-binding predictor (FFT-BP) outperforms all the other eminent methods in molecular biophysics.

The cutting edge of FFT-BP for drug design and discovery is a manifestation of the ever-increasing impact of mathematics on molecular biology and biophysics. There is enormous potential in this area for integrative interdisciplinary research in which mathematicians and experimentalists develop solutions to challenging problems in tandem. Driven by the advances in quantitative and predictive life sciences, MMBB will provide unprecedented opportunities to mathematicians for generations to come.

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Behavioral Ecology

Continued from page 9

Berger-Wolf and her colleagues are creating a dictionary translating GPS and accelerometer data to labeled behaviors such as hanging out, coordinated pauses, coordinated progression, startlement, transition, and unknown. Using new active learning techniques involves exploring the space, optimizing, model-fitting, and eventually inferring and predicting behaviors.

These approaches reinforce the importance of social networks in predicting behavior. Using only a baboon's past history to predict future locations doesn't provide accurate results and implies that social interactions don't matter. The best predictors are simple nearest-neighbor spatial affiliates at short time scales, or animals most frequently near an individual at long timescales (see Figure 1, on page 9). The number of neighbors needed to make a prediction is between four and six for both timescales, possibly defining Dunbar's number for baboons, which is the suggested cognitive limit to the number of individuals with whom one can maintain stable relationships. Coordinated movement of a community is also significant. In higher-order animals, evidence shows that shared decision-making takes place while animals shift from uncoordinated to coordinated movements.

Finding Communities in Dynamic Networks with Graph Cost-Based Methods

Berger-Wolf quantifies social networks of social species, and is the first to examine them from a dynamic network perspective. She begins by translating biologists' questions into abstract problems, and has created a framework for extracting communities and their dynamics in social networks, which identifies the most cohesive persistent grouping with a fluid structure, allowing for membership changes over time (see Figure 2).

Berger-Wolf's method offers much insight into animal community dynamics, indicating which members change affiliations, where they go, when they go, and for how long. As groups split and merge, the model accounts for these real biological events in the form of costs to the community.

Time stamps for networks that change over time must be chosen carefully. When sampling senses data too frequently, such as every second, the data becomes noisy and reveals networks that are too sparse or don't change enough. Aggregating over periods of time that are too long loses important information about the order and causation of interactions. 'Just right' time slices correspond to the temporal scale of the network. Sampling time is a critical part of creating and inferring networks from animal data.

Communities are clusters or subgroups of individuals with relatively strong, direct, frequent ties. The definition of dynamic communities, identities or cohesive groupings that persist over time but with changing members in their clusters, is a little harder to pin down. While individuals are mostly seen with their own community, members of dynamic communities interact more frequently among themselves than with individuals outside the community.

Changing membership in a dynamic community comes with costs: α,α$\beta1$, and $\beta2$. The costαα, for switching communities, occurs because individuals are reluctant to shift affiliations. Switching increases stress hormones, decreases access to resources and the ability to socially share those resources, and drops status. $\beta1$ αand $\beta2$ represent loyalty and loss of social opportunity respectively, $\beta1$ for visiting other communities where more harassment can occur and $\beta2$ for being absent from one's own community.

Animal observation data of physical positions, switches, and visits can yield graphs, the levels of which are assigned to the various costs based on the number of individuals switching, visiting, or absent. A graph coloring problem is an approximable way to model communities, where the colors of individual vertices denote affiliation and the colors of group vertices indicate community structure. The algorithm finds the most parsimonious dynamic communities, minimizing the overall cost across all individuals. The resulting problem is the following: for a given cost setting (α, $\beta1$, $\beta2$), find vertex coloring that minimizes total cost. This becomes a graph coloring problem, which can be approximated close to the optimal solution.

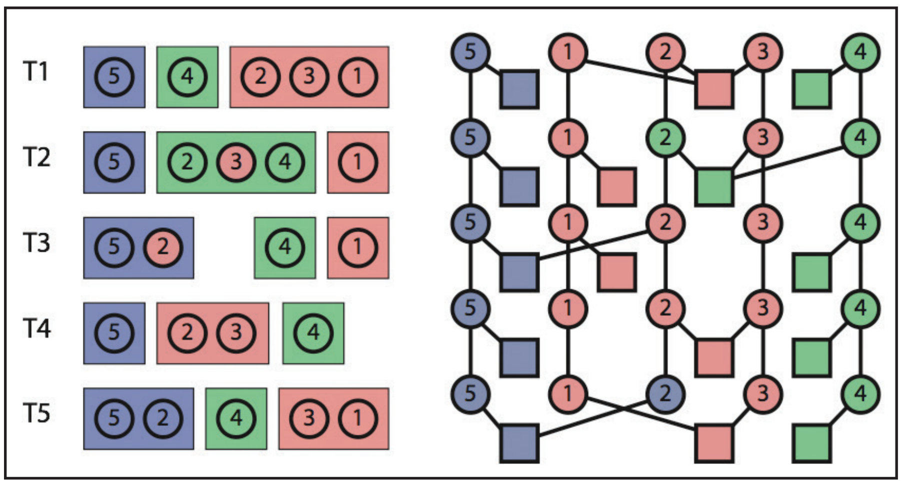

Figure 2. *Framework for identifying communities and their dynamics in social networks. Each color is a community containing individual members.* **Left.** *Example of an interaction sequence between five individuals at five time steps. Each row represents a time step, and time flows from top to bottom. Individuals change associations and groups split and merge. At T1 the red group consists of individuals 1, 2, and 3. At T2, individual 3 visits the green group with individuals 2 and 4.* **Right.** *Corresponding interaction cost graph. The colors show the cost of switching, visiting, and absence. Squares are group vertices and circles are individual vertices. Image Credit: [2].*

Berger-Wolf uses traditional graph theory algorithms to solve these social network problems. "We put standard algorithmic techniques together in a way that's not standard, since the graphs to analyze are nonstandard," she says. Fast flow-based constant factor approximations and cost optimal coloring are also proven maximum likelihood solutions for a dynamic community model.

The graph coloring problem, produced with nine months of aggregated data from observing an entire population of zebras once or twice a day, created a network with definite communities minimizing the overall cost. Principal component analysis (PCA) of the dynamic zebra communities shows four clusters marked by *L*, *N*, *M*, and *B*, indicating that lactating females, nonlactating females, stallion males, and bachelors with diverse resource needs and ways of trading resources all hold different parts in the community structure. This conclusion is biologically meaningful.

Intelligent data collection from GPS collars, drones, accidental photography, cell phone tourist photos, data sensors, and behavior comparison (with genetics and genomics) is creating large data sets that humans can no longer process or find patterns in. Computational techniques, such as Berger-Wolf's work, are already helping analyze and visualize this data to help biologists answer complex questions.

This article is based on an invited lecture by Tanya Berger-Wolf at the SIAM Annual Meeting, which was held in Boston this July.

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Institute for Advanced Study

School of Mathematics

The School of Mathematics at the Institute for Advanced Study has a limited number of memberships with financial support for research during the 2017-18 academic year.

The School frequently sponsors special programs. However, these programs comprise no more than one-third of the memberships so that each year a wide range of mathematics is supported.

Candidates must give evidence of ability in research comparable at least with that expected for the Ph.D. degree, but otherwise can be at any career stage. Successful candidates will be free to devote themselves full time to research.

About half of our members will be postdoctoral researchers within 5 years of their Ph.D. We expect to offer some two-year postdoctoral positions.

Up to 8 von Neumann Fellowships will be available for each academic year. To be eligible for the von Neumann Fellowships, applicants should be at least 5, but no more than 15, years following the receipt of their Ph.D.

The **Veblen Research Instructorship** is a three-year position in partnership with the Department of Mathematics at Princeton University. Three-year instructorships will be offered each year to candidates in pure and applied mathematics who have received their Ph.D. within the last three years. Usually the first and third year of the instructorship will be spent at Princeton University and will carry regular teaching responsibilities. The second year is spent at the Institute and dedicated to independent research of the instructor's choice. Candidates interested in a Veblen instructorship position may apply directly at the IAS website (**https://application.ias.edu**) or they may apply through MathJobs. If they apply at MathJobs, they **must** also complete the application form at **https://applications.ias.edu**, but do not need to submit a second set of reference letters. Questions about the application procedure should be addressed to **applications@math.ias.edu**.

Also, the School of Mathematics is looking for highly qualified applicants in the field of computer assisted formalization of mathematics, univalent foundations and homotopy type theory and is expecting to offer two or more memberships in this area.

In addition, there are also **two-year postdoctoral positions** in computer science and discrete mathematics offered jointly with the following institutions: The Department of Computer Science at Princeton University (**http://www.cs.princeton.edu**), DIMACS at Rutgers, The State University of New Jersey (**http://www.dimacs.rutgers.edu**), and the Simons Foundation Collaboration on Algorithms and Geometry (**https://www.simonsfoundation.org/mathematics-and-physical-science/algorithms-and-geometry-collaboration/**).

School term dates for 2017-18 academic year are: term I, Monday, September 25 to Friday December 22, 2017; term II, Monday, January 15, 2018, to Friday, April 13, 2018.

During the 2017-18 year, the School will have a special program on Locally Symmetric Spaces: Analytical and Topological Aspects. Akshay Venkatesh of Stanford University will be the Distinguished Visiting Professor.

The topology of locally symmetric spaces interacts richly with number theory via the theory of automorphic forms (Langlands program). Many new phenomena seem to appear in the non-Hermitian case (e.g., torsion cohomology classes, relations with mixed motives and algebraic K-theory, derived nature of deformation rings). One focus of the program will be to try to better understand some of these phenomena.

Much of our understanding of this topology comes through analysis ("Hodge" theory). Indeed, harmonic analysis on locally symmetric spaces plays a foundational role in the theory of automorphic forms and is of increasing importance in analytic number theory. A great success of such harmonic analysis is the Arthur-Selberg trace formula; on the other hand, the analytic aspects of the trace formula are not fully developed, and variants such as the relative trace formula are not as well understood. Thus, analysis on such spaces, interpreted broadly, will be another focus of the program.

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The *Institute for Computational Engineering and Sciences (ICES)* at *The University of Texas at Austin* is searching for exceptional candidates with expertise in computational science and engineering to fill several Moncrief endowed faculty positions at the Associate Professor level and higher. These endowed positions will provide the resources and environment needed to tackle frontier problems in science and engineering via advanced modeling and simulation. This initiative builds on the world-leading programs at ICES in Computational Science, Engineering, and Mathematics (CSEM), which feature 16 research centers and groups as well as a graduate degree program in CSEM. Candidates are expected to have an exceptional record in interdisciplinary research and evidence of work involving applied mathematics and computational techniques targeting meaningful problems in engineering and science. For more information and application instructions, please visit: www.ices.utexas.edu/moncrief-endowed-positions-app/. This is a security sensitive position. The University of Texas at Austin is an Equal Employment Opportunity/Affirmative Action Employer.

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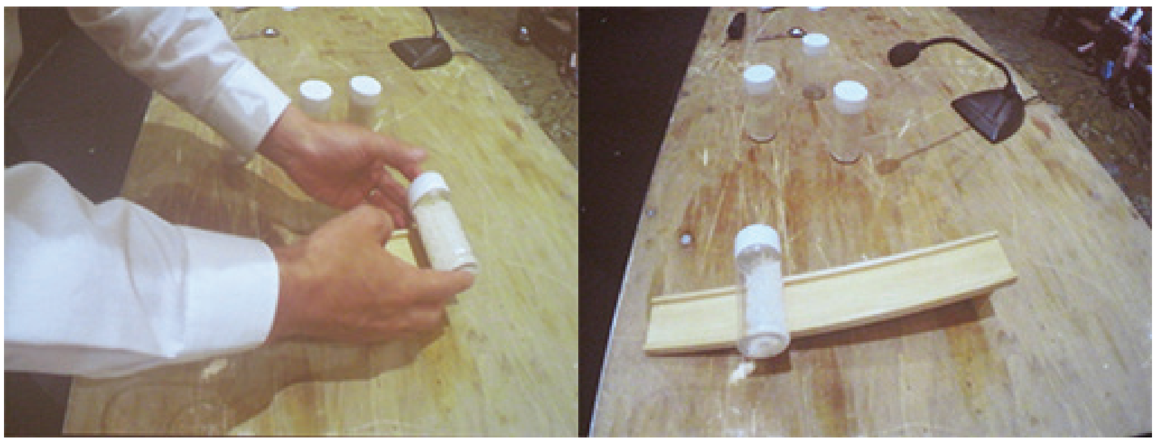
Everyday Objects Make Applied Mathematics Tangible

I.E. Block Lecture Delves into the Science of Toy Models

By Paul Davis



Tadashi Tokieda rolls bottles filled with various amounts of rice down an incline during the I.E. Block Community Lecture at the 2016 Annual Meeting. He explained their movement (or lack thererof) using a property of granular materials: the angle of repose. SIAM photo.

Balls in bowls, dropped coins, tapped tea cups, jars of rice rolling (or not) down an incline…demonstrations, questions, a magician's hands up close on the projection screens, the verbal timing of an improv comic…These are just some of the things that happened at the 2016 SIAM Annual Meeting's I.E. Block Community Lecture.

Tadashi Tokieda (University of Cambridge and Stanford University) used everyday objects to immerse his audience in such central concepts of applied mathematics as inverse problems, singular limits, symmetry, and finite-time divergence. His overarching success was capturing the excitement of exploring, the challenge of discovery, and ultimately the sentiment that "nothing replaces touching," a tenet at the spiritual ground-state of applied mathematics.

Practicing applied mathematicians in the audience who might have spent too long digging at the bottom of their own specialized trench were surely energized as Tokieda rekindled the light that led them into this business in the first place. Non-mathematicians who wondered why their mothers, fathers, friends, or partners worked in this quirky discipline obtained answers that they could see and feel. And all of this came from (mostly) simple, everyday objects that showed the audience that they had "as much access to nature" as the speaker.

Finish your tea, then position the cup with its handle at 12 o'clock. Use your spoon to strike the cup first at 12, then at 3, 6, and 9 o'clock. The sound is the same at all four positions. Why? Then strike the cup at 1:30. How does the tone change? Why does it change?

Can you close your eyes and reconstruct the position of the handle from the sounds produced by tapping? Can sound alone distinguish the original cup from a cup with two half-sized handles at 12 and 6 o'clock?

Tadashi Tokieda charms the audience with visual displays of everyday "toys" during the I.E. Block Community Lecture at the 2016 Annual Meeting. His table-top demonstrations were projected throughout the lecture hall. SIAM photo.

Tokieda identified these two questions as inverse problems, then noted with a smile that you could find "lots of science about inverse problems and lots of SIAM members making their livings" by working on them.

Put three jaw-breaker-sized cedar balls into a cereal bowl, then move the bowl on a table to swirl its contents. The balls circulate more or less independently in the same direction. But shift to eight or more balls in the bowl and they seem to coalesce into a solid that moves opposite the swirl. Presto – a phase change with only a few degrees of freedom.

Two apparently identical heptagon-shaped wheels behave completely differently. When set on their edges and given a gentle push, one advances across the table, though hardly rolling smoothly. The other staggers and falls. What nearly invisible difference produces such radically disparate behaviors? The 7-gon that rolls is imperceptibly flawed: its edges are bowed out ever so slightly and its corners are barely rounded, imperfections just sufficient to permit continuous motion. The falling 7-gon has perfectly straight edges and sharp corners – zero defects, a singular limit at which its staggering collapse bears no relation to the unwavering roll seen in the 7-gon that is close to, but short of, this limit.

Tokieda's table camera focuses on an inclined plane and several cylindrical pill bottles filled with varying amounts of rice. How, he asks, will the rate of descent vary with mass as the bottles roll down the incline? He polls the audience, preparing all for the confrontation between their predictions and the behavior they are about to observe.

The bottle that is two-thirds full moves slowly down the ramp, the rice inside slipping in an avalanche across its free surface while sticking to the wall of the bottle like a viscous fluid.

Preparing to launch the next bottle, Tokieda ceremoniously shoots his cuffs in front of the camera before his magician's hands place a half-full bottle on the ramp. It stalls. A voice in the audience calls out, "Can I change my vote?" A moment later, a nearly empty bottle rolls right down, the few grains in it sliding easily against the bottle's wall like an inviscid fluid.

Unlike a professional magician, Tokieda goes on to explain his trick, beginning with a property of granular materials: the sides of a pile of rice slope at a characteristic *angle of repose*, which depends on the shape, not the size, of the grains. Shallower slopes are stable; steeper ones "landslide" until they attain the gentler angle of repose. Fluids, whether viscous or inviscid, have zero angle of repose: they simply spread into a puddle.

The rolling behavior of a partially-full bottle depends upon the quantity of rice and the relation of the rice's angle of repose to the angle of the incline: if the center of mass of the rice plus the bottle can position itself—if the rice can landslide—so that the force of gravity acts downhill of the bottle's point of contact with the incline, then the resulting torque rotates the bottle down the incline. A lot of rice rolls. Intermediate amounts of rice don't. Very little rice rolls.

Look across the range of bottles from one that is 100% full of rice to one that is totally empty, 0% full; the percentage values that are points of transition between stop and roll, between stationary and moving, are singular limits. Each is yet another instance of the sharp distinctions—like those between viscous and inviscid fluids—that are the meat and potatoes of much of applied mathematics. Here Tokieda displayed them vividly to a large, rapt, laughing audience without demanding the inner vision of a Ludwig Prandtl.

Drop a coin on the floor. It rotates with a clatter that quickly rises in pitch as the coin comes to a stop in finite time. A smattering of physics and some back-of-the-envelope calculus show that the bounce frequency is proportional to an inverse power of $t_{singular} - t$; the divergence in finite time is apparent.

Chattering magnets, crushed paper balloons that are slapped back to shape, and other everyday items offer more evidence of Tokieda's central theme: toys provide a rich ecology of phenomena and ideas, near at hand, awaiting our attention and our touch.

His closing exhortation to "explore and discover" provoked sustained applause, then a torrent of questions. To conclude the questions, he reminded the audience of children who set aside a gift to play instead with its wrapping paper. "We are trained to be interested only in the approved topics," he said. "Make a conscious effort to notice."

No frivolous toys among Tokieda's toy models!

View a photo of Tokeida with his Block Lecture prize on page 8.

Paul Davis is professor emeritus of mathematical sciences at Worcester Polytechnic Institute.