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wisconsin engineer

WINTER 2017 VOLUME 122, NUMBER 1

USE OF CRISPR/CAS9 GENOME EDITING IN STEM CELL BIOENGINEERING

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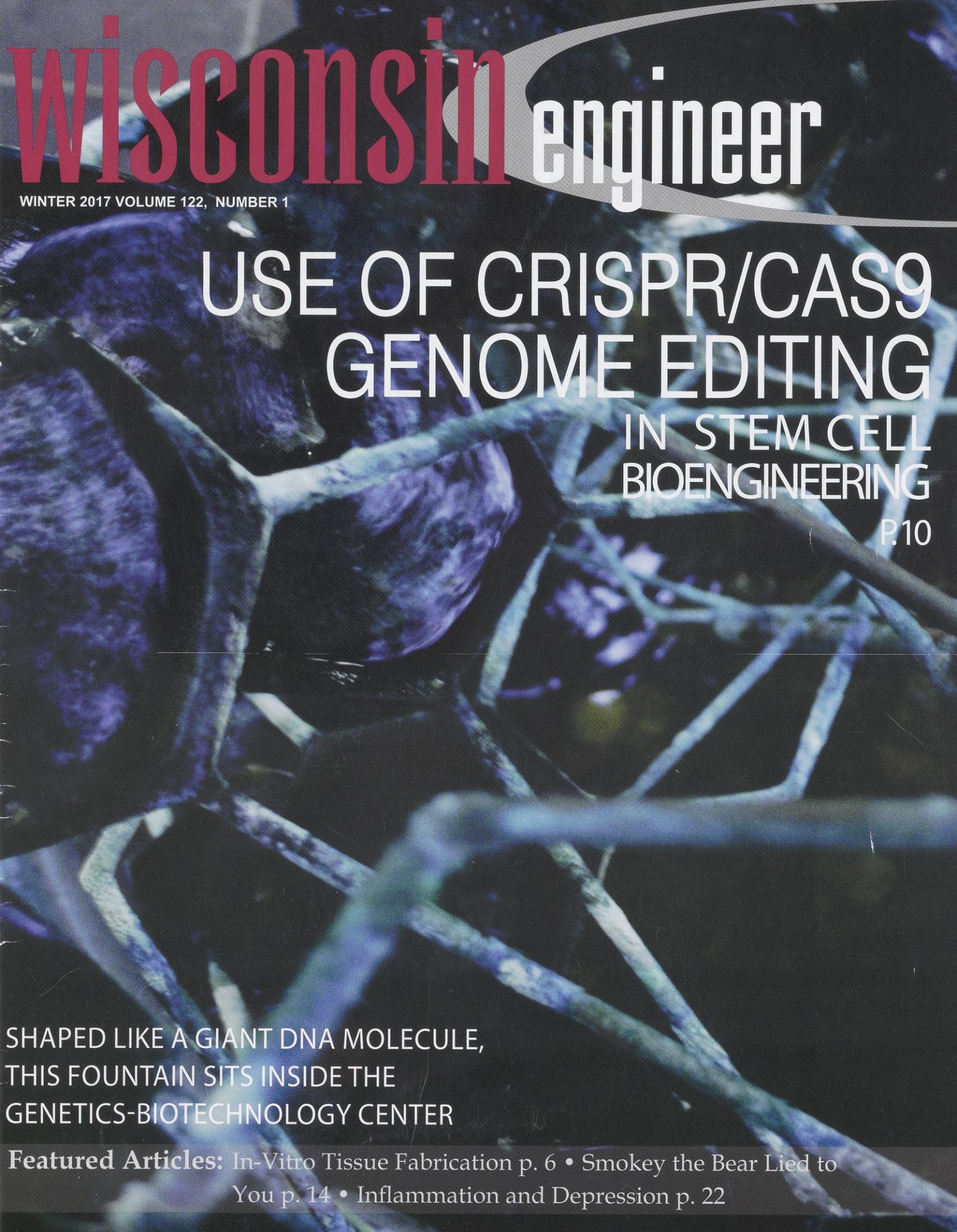

SHAPED LIKE A GIANT DNA MOLECULE, THIS FOUNTAIN SITS INSIDE THE GENETICS-BIOTECHNOLOGY CENTER

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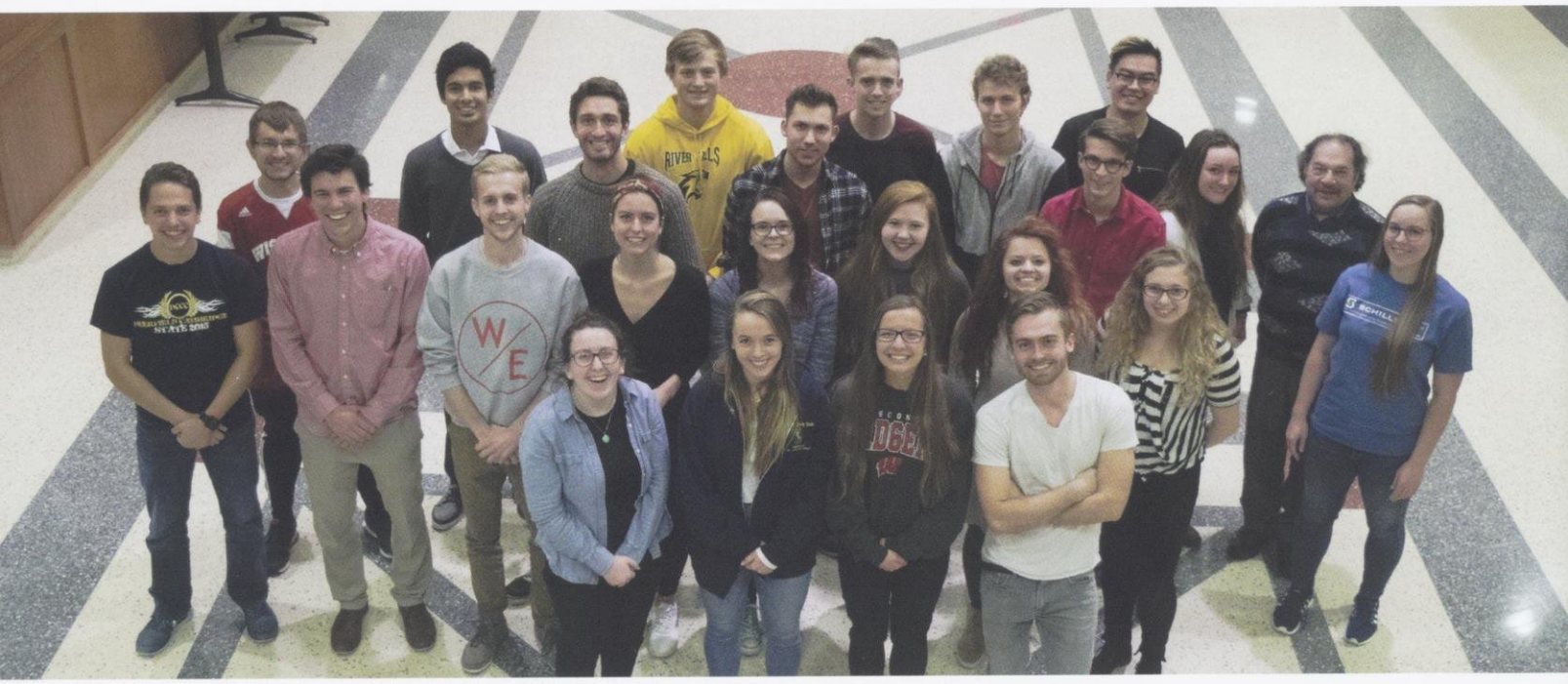

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General

Cover photo by Beth Enright

Madison is Now Home to a New Invasive Species: The Jumping Worm

A new invasive species migrates to southern Wisconsin, quickly causing noticeable ecosystem changes and unknown long-term impacts to southern Wisconsin.

While the Arboretum is home to many species like these geese, the jumping worms are an unwelcome guest.

Invasive species have been wreaking havoc on Wisconsin ecosystems for decades, disrupting our native organisms, and physically altering the environment around us. To make things worse, a new invasive organism was recently discovered at the UW Arboretum in 2013, known as the jumping worm. Formerly only found in the southeastern part of the country, these pests have slowly made their way up to the Midwest, with no intention of leaving. Compared to the common invasive European earthworms, the jumping worms are of Asian descent, found mostly in Korea and Japan.

Jumping worms have an annual life cycle because their cocoons are able to withstand freezing temperatures, allowing them to survive through the winter. The cocoons are brown and about two millimeters in diameter, making them very hard to spot. By late April to early May, the cocoons hatch, and the worms become adults within approximately 60 days. A dangerous trait of jumping worms is that they are parthenogenetic, meaning that they can reproduce without a mate. This means that all it would take is one jumping worm cocoon to start up the population.

Not much research has been done to figure out exactly what impact the jumping worms will have on native ecosystems, especially in the Midwest. Brad Herrick, ecologist and research manager at the UW Arboretum, as well as other researchers from UW-Madison, have assumed the task of studying these new pests to learn about how they can affect our local forest and plant systems, as well as how to eventually control their population. Herrick and colleague Marie Johnston of the UW Soil Science Department have been looking into how heat can affect the jumping worm cocoons by doing experiments with commercial compost, which needs to be heated to a certain temperature to kill off pathogens. They found that all cocoons were non-viable after being subjected to 40°C (104°F) — which is good news since commercial composters are required to heat their piles to a minimum of 55°C (131°F). As long as commercial composters are maintaining their piles correctly, they should be jumping worm-free.

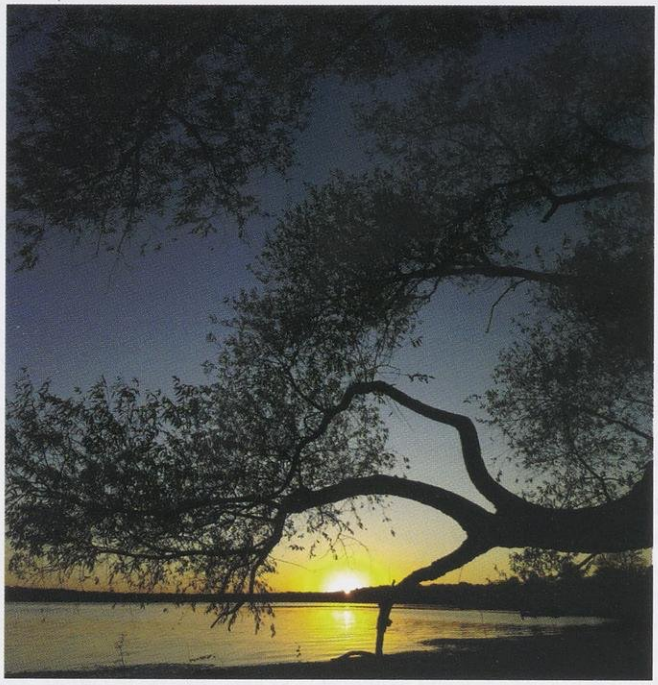
Herrick worked with a former UW-Madison graduate student, Katie Laushman, who chose plots in areas of the forest where the jumping worm is present, and compared these plots with areas that the worm has not yet infested. The researchers were able to tell where the worm was present by looking at the changes in soil structure. In areas the worm is located, the soil becomes much more loose and grainy since the worms consume the organic layer of forests very rapidly, and their excrement becomes the new soil. Another method of figuring out where the worms are located is to make a mustard pour, which involves a blended mixture of dry mustard powder and water that gets poured over the soil. If the worms are present in the soil, they will surface in just a few minutes as the mustard mixture irritates their skin. Herrick uses these locations in order to identify control areas without the worm so he can compare plant communities, soil structure, pH levels, and other variables.

Ever since the discovery of the jumping worms in 2013, the Arboretum has been working closely with the Wisconsin Department of Natural Resources to develop the best practices to mitigate the spread of the species. "Arrive clean and leave clean is one of the biggest methods," Herrick says. Using good gardening practices, such as cleaning tools and shoes before moving to different areas, can be an easy way to help prevent the spread of these invasive pests. "We don't recommend digging up plants from your backyard and bringing them to a plant sale, unless you know for certain that you don't have jumping worms," Herrick says. If planning to relocate or sell plants, a good method to make sure people are not spreading any jumping worms is to bare-root the plant. This is done by washing the roots of the plant until all of the soil is washed away, followed by placing a wet paper towel over the roots to protect them during the transfer.

"Using good gardening practices, such as cleaning tools and shoes before moving to different areas can be an easy way to help prevent the spread of these invasive pests."
– Brad Herrick

Possibly the most important method in preventing the spread of jumping worms is education on what to look for when out in nature. These

worms can quickly change the structure of soil and inhibit the growth of native plants, so it is wise to keep an eye out for any changes in soil composition. Adult jumping worms are easily identifiable by their clitellum, which is a smooth whitish band near their head that goes all the way around their body. With European earthworms, their clitellum is the same color as their skin and only goes around part of their body. Jumping worms also have different behavior than other earthworms such as squirming, slithering, and jumping an inch or more off the ground when disturbed.



Herrick has recently sent out a statewide questionnaire to many environmental organizations around Wisconsin to see where the jumping worm has spread and what people are doing about this invasive species. As of right now, it is believed the jumping worms are only in the southern and central part of the state. During the summer of 2018, Herrick and his colleagues plan to conduct tests with different dosages of an organic fertilizer to see its effects on the worms. This product may end up being something that gardeners can use themselves to reduce the population of these worms.

Continuing on with their research at the Arboretum, Herrick and his team are always looking for interested students to do projects. They are also looking into getting citizens involved in helping them track these invasive species by monitoring the worms at the Arboretum or on their own properties. Working together as a community to mitigate the spread of the jumping worms and many other invasive species can help keep our beautiful Wisconsin ecosystems healthy. So keep your eyes peeled for this new Madison invader, but be careful – they can jump!

Written by: Erin Clements

Photography by: Jason Hakamaki

Design by: James Johnston

The Arboretum has been working closely with the Wisconsin Department of Natural Resources to develop the best practices to mitigate the spread of the species and ensure the area is protected.

Geographic Information System and Applications

It is hard to imagine getting from one place to another without the use of modern technology. Today, most people depend on maps available on their phones to guide them through life. Clearly, cartography and mapping technology plays a vital role in the way in which humans live. Recent advances in technology and computation have given rise to an entirely new field of study: geographic information systems, or GIS for short. The best way to understand what GIS entails is to analyze this acronym by its parts. Geography studies population distribution, climate, resources, land use, and even industry to understand physical characteristics and human activity on Earth as well as their effects. An information system is a way to collect, create, store, process, and distribute information. Geographic information systems are the combination of these things, providing ways to store and distribute information about the physical world and human activity. Through use of GIS, virtual maps are created that make the lives of humans much simpler. Not only is GIS changing the way we navigate, it is also shaping the way we learn about the space in which we live.

Dr. Song Gao, a professor at UW-Madison, says that "location matters in business, intelligence, and even in disaster emergency response," highlighting the need for geographical analysis and the numerous applications of it. Dr. Gao studies two sides of GIS.

The first of these is applied spatial analysis. This deals with technology, innovation, and advancement of geographic systems, such as using cell phones with GPS for navigation. Dr. Gao uses geospatial big data analytics to study human mobility. This geospatial big data can be obtained from mobile phones. WAZE, for example, is a traffic and navigation app that allows the users to contribute data, making it a community-based system. This app gives users an opportunity to volunteer data to help other users decide which route is most efficient in a particular area. The app gives users the ability to inform others of traffic conditions, accidents, and a variety of other things that could be on the roads or causing delays. As Dr. Gao discusses this app, he emphasizes an important question: How can the quality of user contribution be ensured? To explore this, researchers, including Dr. Gao, look at multiple sources of geospatial big data to find commonalities to determine the quality of the data.

The second facet of Dr. Gao's studies implements GIS technologies to identify spatial social problems. "Social media," Dr. Gao explains as an example, "can be used to determine where people are and where people move." Through this, hot spots in human traffic can be located. This could be valuable for businesses as they look for prospective real estate options. Because information like this can be biased, however, Dr. Gao says he "synthesize[s] multiple sources to provide a more holistic view."

Nonetheless, there are still uncharted landscapes that Dr. Gao hopes to realize in his research. As GPS only works outside, indoor navigation is unknown territory in the world of GIS. Dr. Gao decided to take on the task of researching a new and innovative way of creating indoor maps of buildings. By using Wi-Fi routers to apply spatial analysis, indoor virtual maps can be obtained, and three-dimensional surfaces can be approximated. Unfortunately, issues arise when walls and other objects, such as furniture, break the signal. To resolve this issue, a sample of the places can be first obtained to gather information about the distribution of objects in the area. By comparing the similarity of the signal space via Wi-Fi routers to the blueprint of the building, it would be possible to create a useful map. Being able to search the location of a room and having a virtual representation of a building to guide you to the specific room would have many applications. Imagine how much more studying you could do because you no longer need to leave early to find the exam room! This idea could greatly improve productivity in large businesses, too, and all of it is accomplished through pre-existing Wi-Fi routers.

So, what's next with GIS? The goal is to have access to more data faster. Dr. Gao discusses the future with self-driving cars. In order to operate safely, self-driving cars require high-precision geospatial datasets and maps, which contain significantly more detailed road information and the true ground (absolute accuracy) than those found in current conventional geospatial resources for driving. Information about lane location on roads, signs, signals, road conditions, and so many other data need to be readily available for cars to be able to safely drive themselves. Dr. Gao says transportation infrastructure will be crucial for the self-driving car with GIS, providing high-precision mapping used not by humans but the self-driving cars themselves. GIS technology is growing rapidly and will continue to play a large role in the way humans live. Next time you use the map applications on your phone, consider how that system makes your life so much simpler. Remember, the applications of GIS are as limitless as the space in which we live.

Written by: Sarah Gerarden
Photography by: Mayukh Misra
Design by: Patricia Stan

Maps have fundamentally changed the way we view the world and travel.

PRESERVATIVES
& the Truth About Choice

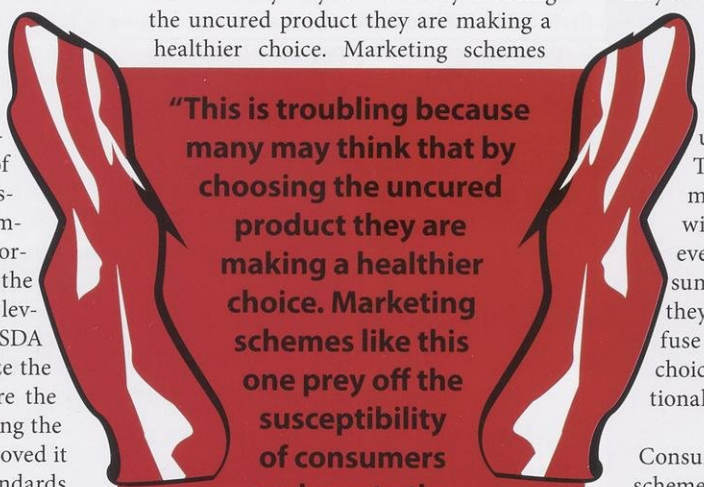
Preservatives have been used throughout history and have become an invisible staple of our diets, so why do consumers fear them and how can this fear be reconciled with scientific data?

When your stomach growls after a long day of work, your first bite is not consumed with the thoughts of "What did I just eat?" You scarf down your meal, and you move on with your day. Rinse, recycle, repeat. However, as consumers, the responsibility to research and comprehend the items we choose to ingest is usually left to us, amidst much conflicting and misleading information.

Although consumers are aware that preservatives are in their food, the science behind them is still misunderstood. A notable example is a preservative called nitrite, a chemically reduced form of nitrate, which is responsible for the flavor and pink color of cured meats. Nitrite is also effective in preventing the growth of pathogens like Clostridium botulinum. However, when combined with certain amines or amides, nitrite has the potential to form nitrosamines, which have been found to be carcinogenic for animals. In the 1960s, scientists realized that these nitrosamines formed when bacon – which contains nitrite – was fried at high temperatures. Despite this alarming discovery, the United States Department of Agriculture (USDA) never banned the usage of nitrite because USDA scientists demonstrated that adding ascorbate or erythorbate during the curing process prevented the formation of nitrosamines when overall levels of nitrite were reduced. Instead, the USDA changed its regulatory policy to minimize the levels of nitrite permitted and to require the addition of ascorbate or erythorbate during the curing process. Even though scientists proved it was safe to use nitrite under these new standards, instances like this one have led consumers to fear nitrite and other preservatives.

Perhaps the biggest scandal associated with nitrites today comes from food companies taking advantage of the consumer's desire to eat healthy food. "[Food companies] are finding natural sources for ingredients consumers worry about, and they are identifying how they can use that source to create the same product," Andy Milkowski says, an adjunct professor in the department of animal sciences at UW-Madison. Most hot dogs, for example, contain synthetic nitrite to preserve the quality of the meat. Some hot dogs, however, are cured with cultured celery powder, which naturally contains nitrite. Both types of hot dogs have similar levels of nitrite, but hot dogs made with cultured celery powder are labeled as uncured. This leads consumers to believe they are eating nitrite-free hot dogs. Even though the consumer believes this to be a healthier alternative, all companies have not switched to this "uncured" hotdog as there may be a slight difference in taste between the two, according to Milkowski. "You don't achieve the same level of accuracy when using the natural source because there may be some contaminants that can cause an odd flavor, for example. Meanwhile, the synthetically-made chemical allows you to dial in what you want to do better which will bring about better results," Milkowski says.

Conflict arises, however, when businesses market these products to consumers as alternatives when at a chemical level they are not. This is troubling because many may think that by choosing the uncured product they are making a healthier choice. Marketing schemes like this one prey off the susceptibility of consumers and create the illusion of choice while taking it away. This is especially dangerous in low-income neighborhoods where choices for healthier alternatives are already very limited. The reality is that without preservatives, like nitrite, food items like cured meats would not be safe for consumption by the time they are bought from the shelves of a grocery store. In a time where very little of our food comes from local sources, preservatives appear to be necessary. Therefore, it is the responsibility of the USDA to use unambiguous language and to close any regulatory loopholes that may provide companies with the opportunity to deceive consumers.



"This is troubling because many may think that by choosing the uncured product they are making a healthier choice. Marketing schemes like this one prey off the susceptibility of consumers and create the illusion of choice while taking it away"

Yet, the real question remains if consumers will ever change the way they choose their food. "It's important that consumers think about what they're putting in their mouths and weigh the consequences. You can try to talk to consumers and point out the science, but it doesn't do much. There's a lot of emotional context with food," says Wendy Bedale, a science writer at the Food Research Institute at the UW-Madison. For example, a hot dog at a baseball game is iconic, and when ordering, consumers usually do not think about whether it may contain nitrite. This is due to the consumer's emotional connection to what may be categorized as the traditional baseball experience. As Bedale mentions, scientific data becomes ineffective when compared to the emotions associated with food because emotions are more easily understood and accepted by everyone. Therefore, in the case of food, it becomes more difficult to reconcile our emotions with scientific data, which may lead to an everlasting battle between the fear the consumer experiences and the types of foods they desire. Ultimately, consumers can refuse or accept these types of foods, but their choices often follow patterns created by emotional contexts.

Consumers should be wary of marketing schemes that take advantage of food trends since consumers are influenced by their emotional connections to food. If the government does not close regulatory loopholes that may lead to misinformed decisions, it becomes the responsibility of the consumers to spread accurate information. As a community of consumers, providers, scientists, and businesspeople, we must all sit at the dinner table and have these sorts of conversations about food to ensure a future of informed decisions.

Written by: Ana Alba
Photography by: Abhi Kumar
Design by: Patricia Stan

IN-VITRO TISSUE FABRICATION

Professor Kristyn Masters explains how modeling diseased tissue significantly contributes to advancements in the medical field.

Professor Kristyn Masters in her lab in the Wisconsin Institutes for Medical Research

Researchers in the field of regenerative medicine have accomplished several noteworthy advancements in the replacement of organs, tissues, and cells severely damaged by illness. However, certain intricate details of regenerative medicine, such as the exact sequence of tissue damage (how symptoms progress, for example), still warrant more observation. The degree of complexity entailed in such work is sometimes subject to undesired results. Because of this, researchers make decisions regarding these mishaps and decide how to best proceed with the research. Professor Kristyn Masters of the Department of Biomedical Engineering confronts similar decisions in her tissue modeling research and exemplifies how these undesired or unexpected results can contribute to significant findings in the field of medical research.

In her initial research (about 13 years ago), Masters' emphasis in the lab was the fabrication of healthy tissue for replacement in case of tissue-damaging illnesses. In the subsequent years, Masters shifted gears to a slightly different type of tissue modeling. One of the illnesses under observation in Masters' lab is Calcific Heart Valve Disease (CAVD), which occurs when calcium deposits clog heart valves and impair their motion. CAVD is primarily treated with heart valve replacement. The first year of Masters' lab focused on engineering these replacement valves. A major unforeseen hindrance would eventually lead to enlightening findings – a recurrence of distorted tissue structures during the fabrication process.

Masters successfully used this roadblock as a stepping stone to her next discovery, which was the importance of observing diseased tissue in the search for more effective treatment methods. "We capitalized on what we were doing so well, which was making these mangled tissues ..." Masters says. She adds that while replacing damaged tissues was a big step, studying the diseased tissue is perhaps more crucial in deciphering the sequences of illness. Knowledge of these sequences can consequently eliminate the need for tissue or organ replacement, extremely invasive processes to the human body. In the case of CAVD, Masters stated, "There are known risk factors associated with [CAVD] such as high cholesterol, smoking, being male or female... we try to put those things together in a dish to understand what comes first..." Masters finally noted that diseased tissue is useful in determining patient variability in response to certain treatment. Through analysis of the tissue and its microenvironment, it has been observed that certain biomarkers dictate the responsiveness to medication for diseases, such as CAVD and cancer and age-related macular degeneration, the leading cause of blindness.

"In the lab setting, we probe more into the causation sequence of disease and through engineering diseased tissues, one can fill in the gaps between different snapshots of the various disease stages."
- Professor Kristyn Masters

The process of manufacturing the diseased tissues and organs is specifically intriguing to Masters. The researchers acquire natural samples from animals (primarily pigs), which serve as templates to create synthetic models due to limited supply and variability. With these complex, recreated models of synthetic polymers, or naturally occurring proteins, they closely mimic the organs and tissues in humans. During this fabrication process, another significant discovery was made regarding the distinction in how male and female tissues responded to disease. Like the damaged tissue, this difference was an accidental discovery while researching CAVD. During the process of observation, some pig heart valves calcified at a much higher degree than others. The researchers initially assumed that some of the heart valves were damaged and ineligible for modeling. Masters suggested the next samples be categorized by male and female pigs. "We found that the male heart valves calcified at a much higher degree than the female ones," Masters says. This observation correlates to the higher susceptibility of the male anatomy to CAVD due the higher calcium content.

Diseased tissue modeling has accomplished numerous advancements in the medical field. Ever moving forward, Masters has a publication in the works providing more detail on deciphering the sequence of certain diseases. Additionally, the lab is making headway in ordering the sequence of disease progression. The discovery that the male and female anatomies have different microenvironments and behaviors down to the cellular level is also starting to gain more interest in the medical research field.

One of the lab objectives is the discovery of factors such as molecules or behaviors that can be inhibited to slow the growth of the disease. The biggest prevailing challenge is determining the right factors without simultaneously destroying the surrounding tissue. Who knows? Maybe this hindrance will be yet another eye-opener for more revolutionary discoveries in medical research.

Written by: Jemimah Mawande
Photography by: Beth Enright
Design by: Patricia Stan

Healthy Eating and Sustainable Practices at the Campus Farmer's Market

More than just fresh produce: the campus farmer's market offers UW–Madison students healthy meal options and sustainable farming practices.

Pumpkins are a popular purchase during the fall.

The campus farmer's market is the perfect place for students to pick up a bouquet of fresh flowers on the way home from class.

The variety of peppers offered at the farmer's market is greater than at local grocery stores.

Fall at Union South! One cannot help but think of students studying, watching films at the Marquee, and having fun at Saturday Badger Bashes. One fall event that few people may be aware of is the Thursday Campus Farmer's Market. From 10 a.m. to 2 p.m., the entrance to Union South is the site of a small yet lively gathering of local vendors. Promoting accessible and healthy produce to students while showcasing sustainable farming practices, this weekly event benefits both students and the community.

Julie Grisa, a marketing major in her senior year, is a manager of the Dining Service Student Project and has been coordinating the Campus Farmer's Market for two years. Grisa says she first became interested in the farmer's market due to her veganism and interest in nutrition. "Vendors have cool insights and offer interesting perspectives on growing their produce," Grisa says.

One way the farmer's market supports sustainability is by inviting vendors that are committed to environmentally responsible farming practices. Parrfection Produce, which distributes produce from local Amish and Mennonite farmers, follows a set of guidelines known as Good Agricultural Practices. Regulated by the USDA, Good Agricultural Practices ensures that the food grown is safe, wholesome, and minimally impacts the environment. In particular, producers are responsible for ensuring that microbial food safety hazards are minimized at all levels of production. To cut down on plastic waste, reusable canvas bags are also distributed during the farmer's market, and discounts are given to shoppers who use these bags.

The Campus Farmer's Market has more to offer than just fresh produce. A variety of other products, ranging from gluten-free baked goods to chili pepper concoctions, are also available to purchase. Every week, campus organizations, such as University Health Services or the F.H. King Students for Sustainable Agriculture, also set up a booth.

To promote student health, the organizers of the campus farmer's market have come up with "Farm-to-Table" bags. Created with students in mind, these bags include both a selection of fresh fruits and vegetables as well as an example recipe that makes use of them. Both the vegetables and recipe included change weekly. From mashed potatoes to pico de gallo, students (as well as anyone else who purchases these bags) can prepare a quick and healthy meal.

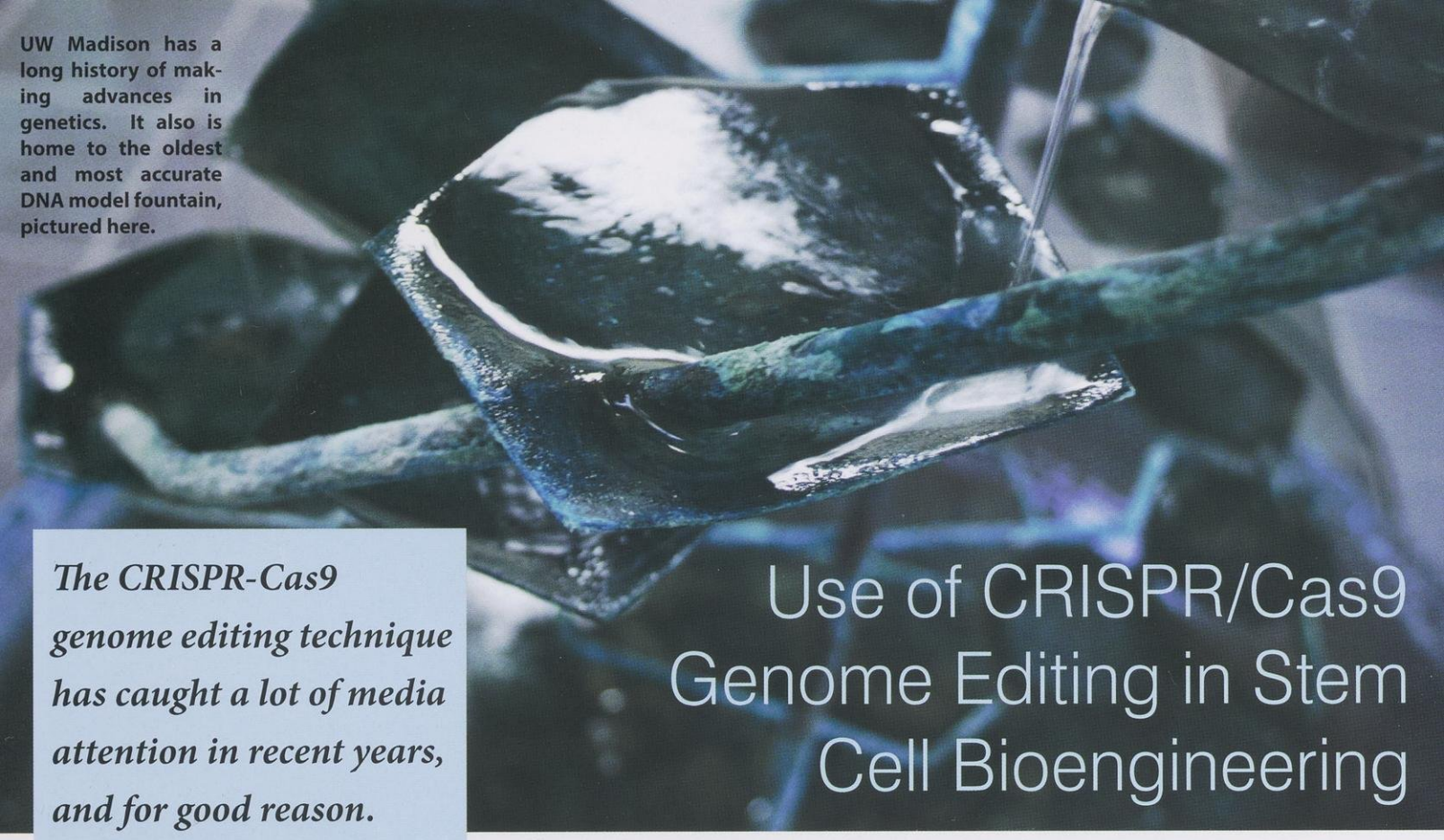
"Variety in food is fun, and the farmer's market is a great way to try and explore new things."
-Julie Grisa

Although there may be some that deride the farmer's market as being too expensive or lacking in variety, a 2011 study by the Northeast Organic Farming Association of Vermont has shown that farmer's markets have comparatively lower prices than their supermarket counterparts. "Variety in food is fun, and the farmer's market is a great way to try and explore new things … through farmer's markets I've eaten foods that I never would have tried before, like kohlrabi," Grisa says. The Campus Farmer's Market is a great way to step a little out of your comfort zone while staying healthy and reducing your environmental footprint.

Written by: Erica Calvache
Photography by: Beth Enright
Design by: Julia Mauser

Students are not only able to purchase a wide variety of food, but also spices to season their meals.

The farmer's market offers a wide selection of products for students to explore that they may not be able to try otherwise, such as spicy scotch bonnet peppers.



UW Madison has a long history of making advances in genetics. It also is home to the oldest and most accurate DNA model fountain, pictured here.

Use of CRISPR/Cas9 Genome Editing in Stem Cell Bioengineering

The CRISPR-Cas9 genome editing technique has caught a lot of media attention in recent years, and for good reason. Scientists are able to make precise genome edits at a low cost relatively easily. This has major applications in the generation of stem cell models and has led to increased lab collaboration across the UW-Madison campus.

DNA contains our entire genetic makeup. Unique to each individual, a genome is like a blueprint, containing the instructions to build a person. Even more important, perhaps, is that our genome harbors the mutations that cause genetic defects. It would seem as though replacing these erroneous genes is impossible, but a new genome editing technique has been developed that may allow for precise repair of these genes or even have us selecting the physical traits of our children in the future. This technology also has the potential to contribute to the cure of many currently incurable genetic defects.

Clustered Regularly Interspaced Short Palindromic Repeats, CRISPR for short, is a new genome editing technique that began hitting research labs in 2012 and has received a lot of media attention since its development. Researchers choose this technique due to its relatively low costs and its ability to make more precise edits. Prior to CRISPR, TALENs and Zinc Fingers were the main genome editing techniques. Both of these systems work well to make DNA strand breaks and conduct repairs. However, these systems are less efficient when attempting multiplexed mutations, which puts a mutation in multiple genes at the same time. These systems also take more time to develop as their structures are more complicated; CRISPR RNA can be made in a lab almost overnight while the prior systems require weeks, months, or even years to generate the necessary specific RNA sequences. With this technology, researchers are given the opportunity to see how far we can engineer a cell and potentially create any DNA sequences to meet any researcher's specific needs.

The system consists of two molecules that introduce a change in the DNA sequence. The first is a piece of guide RNA (gRNA), a pre-designed RNA sequence found in a longer RNA strand. This longer strand will bind itself to a DNA sequence, and the gRNA will guide the second component of the system to the genome site that a scientist would like to edit. The second part of this system is the Cas9 enzyme that acts like a molecular pair of scissors to cut the double strands of DNA at a specific location in the genome. A single cut will be used to drop out a certain gene, such as the peptide sequence that creates the active site of a protein.

At UW-Madison, Dr. Krishanu Saha is using this CRISPR-Cas9 technique in his work with stem cells. Saha became interested in bioengineering while earning his undergraduate degree. During this time, he conducted research on how cells make the decision to become one type of cell or another in a process known as differentiation; this information is not only genetically encoded in the cell but also depends on the environmental factors surrounding the cell. Continuing this work into his post-doctoral research, Saha sought to understand types of genetic information cells have that can be manipulated in the cell. Now Saha's lab is looking at the function of different genetic variance in human stem cell lines and integrating new functions into genomes through synthetic biology. Saha uses CRISPR as a tool to write into the genome effectively and test the functionality of a sequence in human stem cells.

Currently, Saha and his team of researchers are focused on making the CRISPR tool more precise. This technique has yet to be perfected; sometimes other genome sequences adjacent to the targeted sequence or sequences in another part of the cell are changed, so the goal is to better control this. To accomplish this task, Saha's team has spent the last two years attempting to coat the elements of CRISPR with polymers that assist in delivering the system to the right places in the cell upon injection. To make changes to the genome sequence, the necessary proteins, nucleic acids, and molecules need to be at the proper place in the cell. This does not always occur naturally at the desired site in the nucleus. The addition of these decorative polymers to the CRISPR system helps to correctly align each element. Saha's lab has been successful in using this coating method to increase delivery accuracy. Their next step is trying to further understand how the system works and how it will function in different cell types to improve the effectiveness of genome editing.

"As a research tool, it's game changing."

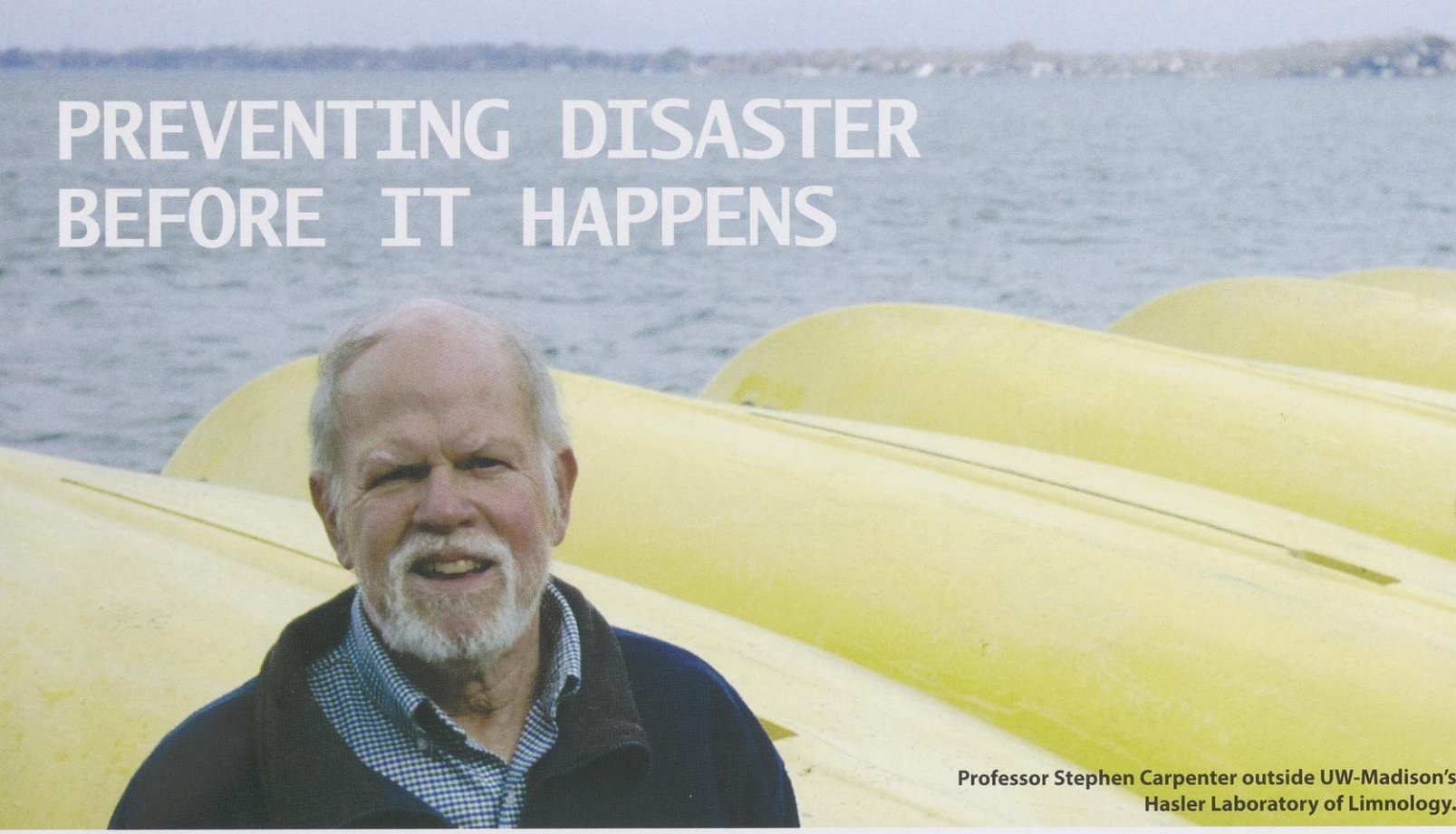
- Dr. Krishanu Saha

Since its development, CRISPR has led to many possibilities in genome editing besides its intended purpose. Researchers, including students, have the ability to look at any gene and make changes in such a short period that collaboration among different labs and projects have begun that would not have, had the technology not been available. These collaborations have changed the way some research is conducted at UW-Madison. One such project is the creation of example tissue cells to use in the testing of toxins. CRISPR is used to tag specific genes with a fluorescent protein that will visibly glow if a gene is turned on or off in the presence of a toxin. This is a noninvasive process that allows medical researchers to better understand toxins and diseases that the body may encounter. Saha has found many successes at his lab here in Wisconsin and sees it as "a great place to work." He continues, "It's rare to have a [College of Engineering] and Biomedical Department that work so well with others on campus, the medical school...the WID (Wisconsin Institute of Discovery), it's been a phenomenal environment for myself and my students." Here at Wisconsin, we've been able to successfully integrate new technologies such as CRISPR and create research connections in the pursuit of exponential growth in discovery.

Written by: Makenna Hall
Photography by: Beth Enright
Design by: Patricia Stan

DNA contains our entire genetic makeup by combining simple building blocks in a double helix, as this fountain models.

PREVENTING DISASTER BEFORE IT HAPPENS



Professor Stephen Carpenter outside UW-Madison's Hasler Laboratory of Limnology.

UW Limnology Professor Stephen Carpenter's Lake Early Warnings experiment and what it means for ecology as a whole.

Though you may not always realize it, ecosystems around us are constantly in flux. Species leave and enter them, weather events change their ambient conditions, and we as humans alter their physical shape through our actions. Over millennia, ecosystems have evolved to cope with these external pressures, but drastic forces may still alter their resting state. For years, scientists theorized that ecosystems might display indicators hinting at these massive shifts. Yet while these theories were shown in experimental settings, ecologists never observed such phenomena on an ecosystem scale – that is, until UW-Madison Limnology Professor Stephen Carpenter conducted his Lake Early Warnings experiment.

Professor Carpenter characterizes stability as a fundamental idea in ecology, describing it as the capacity of an ecosystem to return to a set reference point. The idea of resilience is slightly more complex. In the 1970s, ecologists realized that ecosystems often have multiple stable configurations, and sufficient outside stresses can cause them to cross a "break point" and shift between states. "Resilience is the distance that an ecosystem has to travel or the magnitude of change necessary to cross a break point," Carpenter says. In layman's terms, once the stress is removed after crossing a break point, the ecosystem settles into an entirely different stable state.

Thus, ecologists decided to find these break points. They theorized that ecosystems display general statistical indicators in their populations prior to crossing these break points, namely rises in the intertwined statistical measures of variance and autocorrelation. Variance refers to the fluctuation of a characteristic of the system. Consequently, an increase in variance signals an increase in a system's instability. Autocorrelation refers to the ability to predict a characteristic of the system based on its previous behavior. When autocorrelation is low, the directly preceding data gives little indication of the system's subsequent behavior. "Think of it as the speed the system is moving," Carpenter says. "When autocorrelation is high, the system is moving relatively quickly, and we can see where it'll go next." Ecologists had found the theory to be convincing in small experiments, as they saw rises in both statistical measures before ecosystem shifts. However, they had no way to see if it held true for actual ecosystems. Enter Professor Carpenter and the Lake Early Warnings project.

"All ecosystems have a certain amount of tolerance to changes in the disturbance regime, but all ecosystems have limits, and we're testing and transgressing those limits more and more"

Beginning in 2008, the four-year project studied two lakes in Northern Wisconsin, Peter and Paul, and attempted the unprecedented – to test if the theory of general statistical indicators held true for a full ecosystem. Carpenter's team gradually added top predators (largemouth bass) to Peter while making no changes to Paul, their control lake. As they did so, they monitored chlorophyll levels in the lake to track the phytoplankton population. The team hoped to cause a "regime shift," pushing the ecosystem across a break point and into an alternate stable state. Before the manipulation, Peter's food web consisted of few large predatory fish, many smaller fish, phytoplankton, and algae. After the manipulation, the lake would have many large fish, few small fish, larger phytoplankton, and less algae than before. Moreover, the team expected to see the statistical warnings (rises in the variance and autocorrelation of phytoplankton size) before the shift took place. Yet despite the hypothesis' strong theoretical basis, Carpenter says his team still felt uncer-

tain. "The theory is very strong in the physical sciences, but lakes are very messy systems. A lot of variables are hard to account for, so we really didn't know what to expect," Carpenter says.

By fall 2010, the shift had begun in earnest. Fish traps showed an increase in large predators and a significant drop in the population of small fish, and the phytoplankton had grown larger. More importantly, the team observed clear signals beforehand. Beginning in the spring of 2009, variance and autocorrelation of phytoplankton size began to increase and continued doing so until their peak in early summer of 2010. For the first time, a general statistical indicator of an ecosystem shift had been observed on a full ecosystem scale.

Next, Carpenter's team set out to perform a similar experiment but with an important twist. They would add nutrients to Peter, again attempting to shift the ecosystem, this time in favor of cyanobacteria – toxic algae. However, when warning signs escalated, they would cease the flow of nutrients, testing whether the warning signs indicated an inevitable system shift or were just that – warning signs. "Even though the data ended up taking a few years to fully analyze, we pretty quickly had a good idea of what it would reveal, and seeing if we could halt the shift after seeing the warning signs felt like the logical next step," Carpenter said. Once again, the hypothesis held. When the plankton populations displayed what the team deemed significant increased in variance and autocorrelation, they halted the flow of the nutrients into the lake, and the changes reversed themselves. The phytoplankton population stabilized, and no toxic algae bloom occurred. Moreover, these changes manifested almost immediately – the team observed them the very next day.

The important part about Carpenter's study is what it reveals about ecosystems as a whole. Because his experiment confirms the existence of a general statistical indicator, the results extend beyond just the lakes he studied. "All ecosystems have evolved some sort of resilience, as they've been around for hundreds of thousands of years," Carpenter says. "By comparing the activity of the warning signs in various ecosystems, [ecologists] should be able to discern the relative resilience of the ecosystems." Additionally, Carpenter's work may also give scientists a weapon in the fight against climate change and human-caused ecosystem destruction. His study seems to suggest that by observing warning signs and discerning their cause, the stresses put on the system could be stopped, thus stopping ecological disaster before it occurs. However, Carpenter cautions that climate change alters the drivers of ecosystem shifts. "The problem with climate change isn't that it decreases the resilience of certain ecosystems to change so much as it increases the stresses to unprecedented magnitudes... Ecosystems are no stranger to disturbance, and every ecosystem has a natural disturbance regime to which it's adapted. All ecosystems have a certain amount of tolerance to changes in the disturbance regime, but all ecosystems have limits, and we're testing and transgressing those limits more and more," Carpenter says.

As for what's next, Carpenter has several projects lined up. Currently, he's working with fellow professor Tony Ives and other researchers, analyzing hundreds of sediment cores drawn from lakebeds in an attempt to find the same early warning signs of ecological shifts in sediment records. In the end, however, Carpenter says his heart is set on developing more full-ecosystem experiments. "Ecology is so incredibly scale dependent, so there's always a great need for more large-scale studies."

Written by: Patrick Byrne
Photography by: Simon Hensen
Design by: Patricia Stan

Smokey the Bear Lied to You

Flaws in existing fire management strategies are exposed by a year of unusually extensive wildfires in the West.

Napa Valley, Glacier National Park, and the Columbia River Gorge are just a few of the many areas that have been ravaged by forest fires in the last six months. While the Western and Northwestern United States experience an average of 5.4 million acres of forest fires annually, this year has been particularly devastating. Over 8.5 million acres of forest have been burned, and in Napa Valley alone at least 21 people have died from the blazes. Many of these fires are categorized as megafires, burning at least 100,000 acres of forest. These events have prompted reflection over how and why the frequency of megafires is increasing. They have also encouraged reassessment of fire management policies to ensure responsible protection of human lives and property without unnecessary alteration of forest ecosystems.

The last century of forest fire management in the United States consisted mainly of complete suppression of all fires, treating any burning as a negative outcome. This approach slowly transformed the historically "patchy" structure and distribution of the original forests of the West into the much more uniform, dense forests we see today. Paul Hessburg, a research landscape ecologist with the National Forest Service, explains that "the historical forest landscape was this constantly evolving patchwork of open and closed canopy forests of all ages." This landscape allowed for frequent, but much smaller, wildfires to periodically clear the understory of different portions of the forest without destroying the overstory canopy of the bigger, older trees. In contrast, today's forests often contain high quantities of dense understory growth and slash, a kind of woody debris. These provide easy fuel for the fires and a ladder for the flames to climb up and ignite the overstory canopies of the biggest trees, which were usually safe from the flames of smaller forest fires. The megafires we see today are often created in similarly dense forests.

Fighting these megafires has led to the National Forest Service spending more than half of its entire annual budget on firefighting — over $2.4 billion — in contrast to just 16 percent of its budget in 1995. Skyrocketing costs are a symptom of the extensive damage caused by megafires, but the best treatment is still up for debate. There is a disagreement between two of the main fields of ecology— conservationism and preservationism— over the appropriate policies to adopt. While these fields may seem similar, there are significant differences in their recommendations for fire mediation and forest management in general. Preservationists feel that we should keep human influence separate from nature and designate areas where humans do not interfere. As far as fire management goes, this manifests as a "let it burn" policy, where we allow forest fires to run their course naturally. Conversely, conservationists favor policies promoting a "proper use of nature" which benefits both parties through a coexistence between human development and the wilderness. Conservationists feel it is unreasonable to expect that we ignore the social context and societal influences that govern current fire management strategies.

For conservationists, success in dealing with forest fires is instead measured by ensuring minimal loss of life and property, focusing on preventative policies that allow for establishment of a new status quo. Gavin Jones, a PhD student in UW-Madison's Department of Forest and Wildlife Ecology, falls into this category, explaining that he feels "we need to coexist with nature, not exclude ourselves from nature. But we have a really stained history of doing that well." Jones does research with a team that investigates the effects of megafires on the spotted owl and other old-forest species. The team released a paper in 2016 investigating the threat of megafires to these animals.

Old-forest species such as the spotted owl depend on dense understory canopies for their natural habitats and don't typically live in the more open forests which result from removing understory canopy and brush to help reduce megafires. Unfortunately, forest structures with dense understory are the same ones that are highly conducive

to the ignition of megafires, risking significant high severity burning (burning where 75-100 percent of the canopy has been destroyed). Jones explains that his team investigated the impacts of different types of fires on these species, determining that "fire size doesn't matter… It's really about how severe those fires are." He goes on to explain, "There's actually a wide body of literature that suggests fire is okay for owls-it's good. In fact, our paper also showed that lower severity fire to moderate severity fire, or even small patches of high severity fire [are] totally fine." So, while megafires still aren't an ideal situation, as long as the amount of high severity burning can be minimized, then the fires shouldn't have a detrimental long-term impact.

This is good news for advocates of forest ecosystem restoration efforts like controlled burns, which help mitigate the risks of high severity megafires. It is a delicate task to not only consider the kinds of impacts that megafires can have on humans and wildlife, but also to balance that with the adverse effects human interference can have on natural processes. Ironically, the policy of fire suppression has in fact produced significantly larger, more severe fires than would have ever been possible from natural causes alone. However, Jones' team's paper provides hope that efforts to reduce megafires can help to eliminate the creation of larger patches of high severity fire without necessarily having an extreme negative effect on wildlife. A shift to more preventative techniques like these and the reduction of understory canopies through strategic logging would be steps in the right direction. Unfortunately, before that can happen on a large scale, there needs to be enough interest to provide the necessary funding. Maybe this year's unusually intense fire season will spark engagement from the public in ways that have never been seen before, leading to a solution we all are okay with implementing.

"We need to coexist with nature, not exclude ourselves from nature. But we have a really stained history of doing that well."

Written by: Ben Zastrow

Photography courtesy of Sheila Whitmore and Danny Hofstadter

Design by: Jonathan Evans

Dr. Pete Mcintyre in front of the Hasler Laboratory of Limnology on Lake Mendota where he studies the effects of dams on biodiversity and the environment.

Semi-Green Technology

The blind acceptance of renewable energy sources being environment-friendly may disregard the more complex environmental, economical, and social impacts of these developments.

The outward expansion of land development is putting an increasing strain on both availability and quality of natural resources. To combat this trend, there has been a push toward implementing renewable energy systems that can support the rising energy need in developed and developing regions, while protecting and preserving our limited resources. Unfortunately, the benefits of this "semi-green technology," as Dr. Pete McIntyre of UW-Madison refers to it, are often accepted without accounting for the potential impacts on local biodiversity, agriculture, and sociopolitics.

A key renewable energy system utilized today is hydropower. One pressing issue associated with the building of dams and other hydropower structures is the altering of the natural river processes and therefore the local ecology. This problem is compounded by the fact that the areas of highest biodiversity are also often the areas seen as most efficient for hydropower. At UW-Madison, McIntyre and his community within the limnology department are particularly concerned with the impact these technologies are having on their surroundings. "You have specialized species; you have a very small area that they're restricted to… and those are the areas that we tend to mess up the most," McIntyre says.

Many of the fish species in large volume regions of rivers, where dams are often built to maximize energy output, are only able to live in these streams above a certain threshold volume. This is a great danger in areas like the Mekong River Basin in southeast Asia, home to over 1,000 species of fish and invertebrates as well as an active site of hydropower development. Many of these fish species depend on migration across miles of river channel to complete their life cycles. By more closely examining the species present in areas of proposed dam building, McIntyre hopes to provide government agencies and engineers with information on the least damaging areas for dam construction. "We're not anti-dam, we're pro-smart dam," McIntyre says. This line of reasoning follows in other renewable energy systems as well. Implementing these systems requires research and forethought to avoid unintended consequences on local biodiversity and other negative environmental effects.

Areas such as the Congo and Ethiopia are still in the developing stages of widespread energy use. The hope in these areas is that reliable sources of power from hydroelectric dams will lead to increases in education, a higher standard of living, and a place in the profitable international energy market.

However, it is conceivable that there could be unintended side effects upon construction. Consequences of these dams extend just beyond threats to biodiversity. At UW-Madison, Professor Paul Block studies the many impacts that dam construction may have on local agriculture and the "hydropolitics of the Nile," as Block refers to it.

A proposed dam to be completed in summer 2018 in Ethiopia will be the first of its size on the Blue Nile and poses potential issues. The building of the dam and reservoir will alter the flow of the river and regulate it for steady power production. While this may seem like a positive outcome, "sometimes we're solving one problem and we're actually creating another one," Block says. The natural flooding of the plains around the river provide annual renewal of nutrients and ensure reliably productive soil. Removal of this ancient agricultural technique will have a significant impact on the practices of farmers in the area.

Additionally, Egypt will likely receive less freshwater as Sudan diverts it upstream as a steady source of water for irrigation. In the face of these changes, engineers like Block develop precipitation prediction models that can provide farmers with insight on the upcoming growing season in order to "mitigate their vulnerability to variability," as Block says.

In the case of several hydropower systems, fewer fish are able to complete their migratory cycles and die out. Because of this, there will be less seafood available for trade and sale on the market, damaging the economic vitality of the fishery. More importantly, there will be less fish available as a food source for local communities. Thus, not only will the dams be impacting the well-being of the fish but also the locals, as "you're undercutting their food supply," according to McIntyre. In the act of supplying power to these people, their livelihoods may be put in danger. These systems not only affect the environment of their immediate surroundings but the local, and even global, economy as food security, livelihoods, and job growth in related industries are affected.

Ultimately in regard to energy system planning, this research serves as "another piece of the puzzle," Block says. Both professors see their research as only "one of the many elements in planning the future of hydropower," McIntyre says. With our consumption of energy still on the rise, more renewable systems, including hydropower, will be built. In order to maintain an ecological balance that can be sustained, energy system planning and careful forethought will become even more paramount, especially in the developing regions of Asia and Africa. "All of these anthropogenic changes are having real ecological impacts," Block says. Hopefully through the work of many engineers and scientists, new information can be used by policymakers to best express local and global interests of citizens and their environment.

Written by: Katlyn Nohr
Photography by: Jason Hakamaki
Design by: Jonathan Evans

Small Fruit, LARGE IMPACT

"The recipe wasn't quite right," says Dr. Shawn Stephens, a researcher at UW-Madison, speaking about cranberries. This comment, however, does not refer to a recipe that is made to complement a steaming slice of turkey on Thanksgiving—Stephens refers to the recipe of pheromones he uses to help stop pests, like moths, from eating the valuable crop. At UW-Madison, Stephens works to protect cranberries, the most important fruit industry in Wisconsin, by implementing new techniques in crop protection.

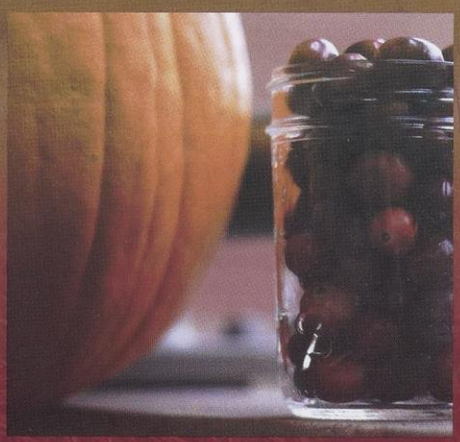
"It is the most important fruit crop in the state, and it supports tens of thousands of jobs."
- Shawn Stephens

Unbeknownst to the average Wisconsinite, cranberries are key to the identity of Wisconsin as the state provides over 60% of all the U.S. production of cranberries. This industry is worth $350 million to the state. "It is the most important fruit crop in the state, and it supports tens of thousands of jobs," Stephens says. Cranberries are the cornerstone crop to many communities in central Wisconsin and sustain entire counties such as Monroe and Juneau.

Wisconsin is geographically blessed to have such a large impact on cranberry production. In south-central Wisconsin, a large quantity of the land is marsh. Little else can grow in this region but moss, shrubbery, and cranberries. The soil is highly acidic, and this land has little residential development value because of the poor soil structure. Yet, there is plenty of water to use for harvest. With these conditions, Wisconsin finds itself in a prime location for this crop, allowing this industry to flourish in what otherwise would be little-used countryside.

Cranberries digress from most prototypical fruits by the way they are harvested and consumed. Unlike most fruit, only five percent of cranberries are purchased raw, as most people prefer to eat the fruit in juices or dried. What also sets the berries

Cranberries not only make an impact in a great holiday meal, but they are part of the identity of the state and an important area of research at UW-Madison.



Cranberry Bog at Hook Lake Bog State Natural Area. While it might not look like much in the off season, this cranberry bog is alive with bright red and burgundy hues during harvest. Hook Lake's cranberry bogs feature a diverse ecosystem of aquatic vegetation including paper birch, bogbean, leather-leaf, and, of course, cranberry!

apart is their unique way of harvesting, which involves flooding the fields, called bogs, with water. This uncommon technique can be realized because of the cranberries' four hollow cavities in the center of the fruit which allow them to float on water, enabling easy collection.

Stephens and other researchers at UW-Madison protect this crop by mitigating the impact of harmful moth species through the application of sustainable and environmentally-conscious processes. These moths pose a threat to cranberries when they reproduce and lay eggs on cranberry fields. After their eggs hatch, the larvae feed off the cranberry plants until they are ready to grow and metamorphose to later stages. Researchers have worked to mitigate the damages associated with this process. To do this, researchers use a technique called mating disruption, which involves infusing wax with female moth pheromone that can be spread throughout the crop fields. When mating season begins, called "flight," the males can't find the females because the bogs are covered in a giant cloud of female pheromone, decreasing the amount of eggs being laid. The consistency of this wax sounds less than desirable, in Stephens words, "it's like a yogurt wax soup." Stephens helped bring this pest mitigation technique from the Northwest to Wisconsin. This process is not unique to cranberries, as Stephens says, "Most of the apples that you purchase and eat have been grown under mating disruption."

According to Stephens, the mating disruption technique is much more effective than spraying pesticides and better for the environment as well. Stopping moths can be hard, and with more traditional techniques it takes precise timing of the life cycle of the moth. Favorably, these dollops of wax can be applied at a less specific time and are much more effective, while doing little harm to the environment. The dollops of the waxy substance eventually break down into miniscule pieces and integrate into the soil.

Researchers like Stephens protect one of the most important products to the state. Work like this sustains more than just cranberries, as it preserves aspects of Wisconsin's culture, economy, and identity. Politics aside, the public funding UW-Madison receives has direct impacts to many small subsets of the state like cranberry growers. Next time you give thanks over a slice of turkey, remember that researchers at UW-Madison are part of the process that helped make this delicious celebratory meal.

Written by: Ben Hayes
Photography by: Mary Shaughessy
Design by: Patricia Stan

Professor Matt Allen with an artist's rendition of a rocket at takeoff. Forces during this stage of space travel are a major focus of his research.

Structural Dynamics Analysis of the Space Launch System

A peek into the analysis and planning vital to make a rocket mission successful.

Hearing the words "NASA" or "rocket ship" probably conjures images of large-scale mechanical systems like the space shuttle or the International Space Station. To the casual observer, the term rocket science may just seem like a far-fetched concept that would not play a significant role in their day-to-day life. However, have you ever stopped to think about the amount of thought and effort that goes into designing, building and testing projects that are this large of scale? NASA's Space Launch System (SLS) – the massive rocket capable of propelling humans and cargo to the ends of the universe (or at least Mars) – is no exception. Significant research and testing is required for everything from the propulsion system to the structural integrity of a single bolt. One such vital area of analysis is structural dynamics which analyze the loads and vibrations of a system as it is in motion. This is such a critical analysis because of the severity of the damage if anything goes wrong. If the load exceeds the strength for even a single bolt, the impact, and the consequences, could be catastrophic.

UW-Madison Professor Matt Allen from the Structural Dynamics laboratory has been working with NASA to ensure the best possible methods are being used to test and model the SLS. In general, the laboratory and Allen's research aims to model complex systems to predict the response and stresses during dynamic events. These predictions certify a better understanding on how to design these systems. The engineering analysis that goes into these models is, of course, much more complicated than what would be found in the basic statics course that UW-Madison engineering students take, yet the same fundamental principles apply. Something as seemingly trivial as a single bolt failing because the actual in-flight stress is higher than predicted could lead to mission failure. Allen preaches that every component in the system is as important as the next, and nothing can be neglected during the designing and testing procedure. An engineer with over 30 years of experience at the Aerospace Corporation has said that this is the most complex vehicle ever to be built. "You can't design a rocket like this by trial and error. We have to know that it will work the first time, or there will be some incredible fireworks on launch day and the potential for loss of life or other serious consequences," urges Allen.

"Without this type of research, you can't hope to speed up the process of building a rocket"

In many cases, especially in an assembly as complex as the SLS, the computer model itself is not sufficient proof that the rocket will survive even getting out of Earth's atmosphere. The rocket shakes with the greatest intensity at a point called "max Q," (or maximum aerodynamic pressure) in which the speed of the

rocket and the atmospheric density combine to produce the worst-case aerodynamic loading for the rocket while still in the earth's atmosphere. Many failures can take place at this instant. If, for example, a resonance is excited—a case where the forces a system experiences are at exactly the right frequency to accentuate the response of some mode of the system. This is analogous to pushing a child on a swing; if they're pushed at random, they don't go very high, but if they are pushed, even a little, at just the right interval, then each push builds on the last and the swing rises high. The resonant or non-resonant shaking could also cause nonlinear effects, especially in joints, which are currently very difficult to model in computer simulations. Thus, researchers and engineers must empirically find the balance between testing and simulation to create the best rocket possible. "The design process involves tradeoffs between analysis and testing to check the analysis and fill in knowledge gaps, and all of this has to be balanced with cost and schedule to deliver the vehicle on time – or, let's say somewhat in the ballpark of on time," says Allen, with a grin.

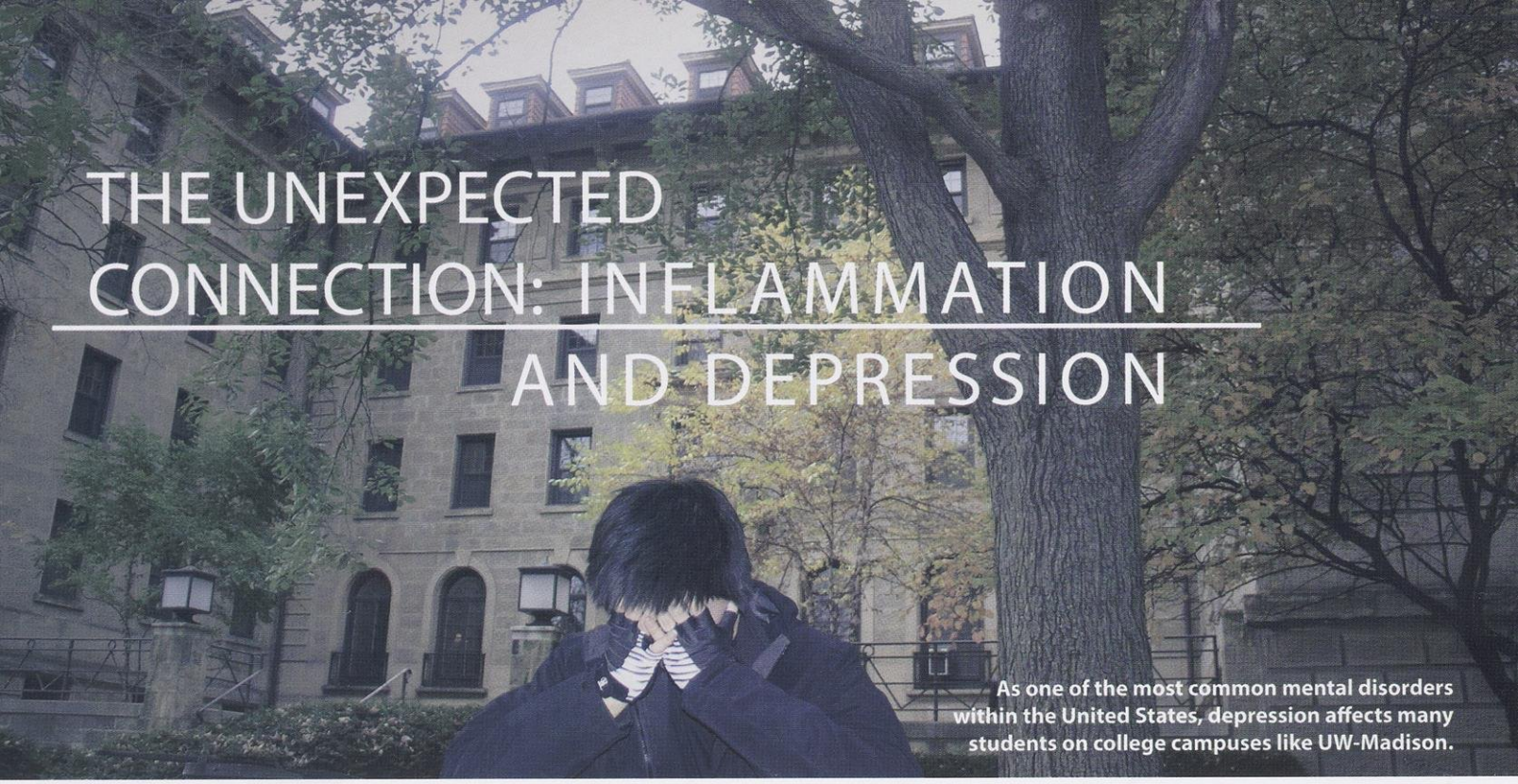
All of these efforts must consider cost effectiveness because, compared to the development of the space shuttle in the 60s, this project must be done on a shorter timeline and with far less money. With these constraints as well as the inability to perform extensive testing and scale models for the rocket as was done for the shuttle, the structural dynamic analysis becomes even more important. "Without this type of research, you can't hope to speed up the process of building a rocket," explains Allen.

When the space shuttle was built, NASA had a dedicated testing facility with equipment to lift the entire vehicle, so it could be tested in a freely hanging configuration, which is similar to the flight condition. Due to the tighter budget with SLS, it won't be possible to renovate that facility, and no other facilities exist that can lift a multi-million pound, 300 foot tall flight vehicle. So, Allen and others are working to devise other tests like when the rocket is mounted on the launch platform. This test can be used to check the validity of computer models. This proves more difficult than one would think because every vibration of the rocket causes flexure in the entire launchpad, making it necessary for the entire system, launchpad and all, to be modeled with the same care that is given to the flight vehicle. Taking out the dynamics of the tower and platform and only focusing on the dynamics of the rocket proves to be a difficult task. As such, this is something NASA has never done before and Allen is working to test the feasibility of these ideas.

This process, seemingly simple on the surface, takes many years to perfect because so much planning and analysis must take place in every step. The challenge is in every component being designed specially to undergo the types of loadings and vibrations that it will experience during launch. "If you were to take a standard iPhone and bolt it into the [rocket] bay, would it survive the ride? Probably not," says Allen. As testing and analysis continue for the SLS less than one year from its anticipated November 2018 launch date, many people are tirelessly working to make sure that this mission is a success as it could be the start of a new age in space exploration.

Written by: Jordan Wolff
Photography by: Jason Hakamaki
Design by: Patricia Stan

THE UNEXPECTED CONNECTION: INFLAMMATION AND DEPRESSION



As one of the most common mental disorders within the United States, depression affects many students on college campuses like UW-Madison.

Breakthrough studies in depressive disorders suggest a link between depression and inflammation as well as potential treatment strategies

Depression is one of the most common mental disorders within the United States. It is an illness that affects mood, emotions, and behavior, which can make day-to-day life for diagnosed individuals extremely difficult. According to the National Institute of Mental Health, over 16 million individuals over the age of 18 suffered from at least one form of a major depressive disorder in 2015, making depression one of the most common forms of mental illness[1]. The various forms of depression (including major depression, dysthymia, postpartum depression, atypical depression, psychotic depression, and bipolar disorder) originate from a number of sources including fluctuations in hormone levels, stress, grief, and substance abuse[5]. However, researchers are still working toward more exact causes and how to treat them[2].

Recent studies have revealed that one possible source for at least some forms of depression may be inflammation throughout the body and brain. The body becomes inflamed when trying to fight off an infection, such as one brought on by a common cold or the flu. Inflammation is the body's response to stress, whether it be from diet, environment, or lifestyle[6]. For example, in the case of a cold, inflammation may occur through a fever, which heats up the body and helps to prevent what is invading the body. In depression, the inflammation is caused by stress that raises cortisol levels within the body. Cortisol, which is often referred to as the "stress hormone," is involved in blood sugar regulation, metabolism, memory formulation, and the reduction of inflammation[7]. The inflammation causes symptoms such as disrupted sleep, mood swings, fatigue, foggy-headedness, and impaired concentration[3]. For a cold or flu, these symptoms are not persistent and typically subside in a few weeks. In the case of chronic illnesses such as Parkinson's disease, cerebrovascular disease, or multiple sclerosis[8], the majority of the symptoms can potentially last years. As a result, many individuals suffering from an inflammatory chronic illness exhibit similar symptoms of depression.

One of the more significant discoveries regarding inflammation and depression links the two to early-life adversity. Early-life adversity often includes abuse, chronic neglect, economic hardships, or lack of adequate support. These factors may disrupt the development of the brain and increase the risk for stress-related disease[9]. One study conducted by UW-Madison Professor Charles Raison suggests that individuals who suffer from early-life adversity are often in "chronic" states of stress, which in turn cause spikes in the inflammatory response[4]. The spikes, followed by bodily inflammation, seem to predispose or predict the likelihood of depression later in life. However, the reverse process would not necessarily occur. While inflammation and depression are correlated, they are independent of early-life adversity; it is simply the overactive inflammatory response caused by early-life adversity that predisposes one to stress[4].

While this area of research is still a work in progress, the defined link between inflammation and depression opens many doors for new medications and treatment plans specific to certain types of depression. Anti-inflammatories, such as omega-3 essential fatty acids, may be used to help decrease levels of inflammation and mitigate the effects of depression[4]. This is promising for depressed patients as well as those suffering from chronic illnesses.

While these treatments continue to be improved, one should not haphazardly use anti-inflammatories, as they could potentially aggravate or worsen the inflammation. Anti-inflammatories, in the case of depression, refer to very specific types of drugs, such as anti-cytokine antibodies, not typical over-the-counter anti-inflammatories such as Tylenol or Ibuprofen[10]. Using improper anti-inflammatories that are not specifically prescribed by a health professional could in turn have negative consequences. While there is still much to be learned, the research linking inflammation to depression may lead to treatments for those suffering with certain forms of depression and establish a better understanding of depression as a whole.

Written by: Lucy Shoemaker
Photography by: Gary Geson
Design by: Patricia Stan

View citations for this story at www.wisconsinengineer.com.

Updating New Software Can Bring IoT on a Higher Security Level

We're moving closer to the widespread network called the Internet of Things (IoT). With this system, we're also moving closer to the benefits and threats it can bring us.

From rental bikes to refrigerators, more devices are connected to the internet every day. With this system, we're moving closer to the widespread network called the Internet of Things (IoT). Even more so than in consumer devices, IoT is finding use in diverse commercial industries. IoT is not exactly a new concept, as people have been theorizing about its applications for decades. These realizations of IoT have brought us vacuum cleaners that clean the house daily, coffee machines that prepare coffee as users wake up, and refrigerators that order groceries for them.

IP cameras have been susceptible to security exploits resulting in DDoS attacks.

The IoT technology is even more promising for the business sector than for consumers. "In the consumer domain, benefits of IoT are not completely clear. They create some convenience but not much beyond that. However, the situation with business and industries are little different, and there are more opportunities for IoT usage. Businesses depend on efficiency and take advantage of economies of scale," Computer Sciences Professor Bilge Mutlu says. Although IoT has been discussed for over two decades, there still are limited applications. The technology is facing many challenges as industries insist on more complexity, but perhaps the biggest challenge for IoT is security vulnerability. This vulnerability can be caused by different factors that are related to IoT update software, old internet sensors, or machine authorization.

Since companies continue to use old internet devices and network connections, IoT is constrained from reaching a higher security level. Internet sensors that are currently used for machine-to-machine communication use old hardware, leaving them more vulnerable for hacking. Constant updates are required to secure IoT systems, which could increase maintenance costs well beyond mechanical maintenance on machines. "The number one thing IoT vendors and service providers can do is design their devices so they are patchable by end users — meaning that when security vulnerabilities are discovered, they are able to be updated with security fixes, preferably automatically," says Dave Schroeder, an information technology strategist at UW-Madison. "Users can look for devices from vendors that provide security updates and have a proven track record on security and privacy." This requires IoT service providers to constantly monitor potential hacks, as well as constantly improve their system.

Consequently, there have already been cases of failed IoT security systems. For instance, inexpensive Chinese-made IP cameras and devices like set-top boxes became part of the Mirai botnet, which were involved in widespread distributed denial of service (DDoS) attacks in 2016. Those devices did not have proper security updates, and the vulnerabilities could not have been patched. "When price and features are the only criteria for a customer, security is often overlooked," Schroeder says. "On the contrary, some companies were able to implement an IoT high security system into our lives." To contrast, we are definitely able to see some companies successfully implementing their IoT with high security level. "Examples of good practices with IoT products are Google's Nest smart thermostat and Amazon's Echo devices. Both vendors deliver timely security updates for these devices, and they are installed on the devices automatically." Another good example is the modern smartphone — we take these for granted, but they are another part of the IoT with successful security updates.

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A specific security challenge that should concern IoT providers involves machine authentication, which is the authorization of a machine-to-machine communication through verification of a digital credentials. With IoT implementation, the devices communicate with each other, so one machine should be able to authorize another one in a secure manner. With AI development, machines will be able to program system updates for each other, allowing IoT systems to communicate more securely.

No matter how fast IoT systems progress, system providers should focus on upgrade potential to ensure high quality security is included with the product. Ultimately, regular system upgrades will allow the implementation of new features on the IoT system, creating benefits for both businesses and consumers.

Written by: Yuliia Kapeliushna
Photography by: Matt Henricks
Design by: Patricia Stan

Robots that autonomously vacuum are one realization of IoT that consumers can experience.

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