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The Arkansas Catalyst

July 2013

Probing for Answers

Julie Stenken, Twenty-First Century Chair in Proteomics

Proteomics is the large-scale study of the structure and function of proteins. Julie Stenken, professor of chemistry and biochemistry, is leading a research team that received a four-year, $1.3 million grant from the National Institutes of Health to study the "foreign body" response to implants.

The challenges scientists have faced in developing reliable implantable glucose sensors are two-fold: the sensors must deal with the foreign-body reaction, where a person's body attempts to wall off the implanted material from healthy tissue, and just as importantly, blood chemistry and tissue vary from person to person. After a week, these natural phenomena cause erratic glucose readings from sensor implants, Stenken said.

"The whole foreign-body reaction drives a series of immune responses that then serve to encapsulate the sensor away from healthy tissue," Stenken said. "This sensor is measuring glucose in an encapsulated 'bag' around the sensor rather than being able to sense what is out in healthy tissue. That becomes an extremely dangerous situation clinically, because if you dose with insulin when you don't need to, the person can go into diabetic coma or eventually death due to an inaccurate reading from the sensor."

Stenken is a leading expert in the area of in vivo (in the body) collection of proteins known as cytokines using a technique called microdialysis sampling. Her aim is to understand the inflammatory response caused by cells called macrophages to implanted foreign materials.

Stenken is collaborating on the grant with Jeannine Durdik, professor of biological sciences and assistant dean for research in the Fulbright College of Arts and Sciences, and Liping Tang, professor of bioengineering at the University of Texas at Arlington.

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University Honors NSF CAREER Award Winners

The University of Arkansas held a reception at Wallace W. and Jama M. Fowler House on June 5 for faculty who have been awarded funding by the National Science Foundation through the Faculty Early Career Development Program, better known as a CAREER award.

The office of vice provost for research and economic development sponsored the event, which honored university faculty who received CAREER awards. The university has received 27 CAREER awards since the program's inception in 1992, and is currently home to 19 awardees.

The CAREER award is one of the highest honors given by the foundation to junior faculty members. Recipients are selected based on high-quality research and the integration of that research with education initiatives in the context of the university's mission. The award provides a minimum of $400,000 support for five years, or five years and $500,000 for those in biological sciences or polar programs.

Faculty who have received CAREER awards who are currently at the U of A, listed in alphabetical order: Laurent Bellaiche, physics; Luca Capogna, mathematical sciences; Greg Dumond, geosciences; Julian Fairey, civil engineering; Ingrid Fritsch, chemistry and biochemistry; Colin Heyes, chemistry and biochemistry; Russ Meller, industrial engineering; Lin Oliver, physics; Xianghong Qian, chemical engineering; Doug Spearot, mechanical engineering; Julie Stenken, chemistry and biochemistry; Susanne Striegler, chemistry and biochemistry; Jak Tchakhalian, physics; Paul Thibado, physics; Feng Wang, chemistry and biochemistry; Ranil Wickramasinghe, chemical engineering; Shui-Qing “Fisher” Yu, electrical engineering; David Zaharoff, biomedical engineering; Nan Zheng, chemistry and biochemistry; and Min Zou, mechanical engineering.

Genders Communicate Consent to Sex Differently

A University of Arkansas researcher’s work on the way men and women communicate their consent to have sex

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GRANT AWARD WINNERS

The following is a sampling of faculty awards in June, with the principal investigator, the award amount and the sponsor. An asterisk (*) indicates the continuation of a previous award.

• Frank Millett, $1,042,877, National Institutes of Health*
• Fisher Yu, $300,002, Defense Advanced Research Projects Agency

could lead to improved sexual assault prevention programs on college campuses.

Kristen Jozkowski

Kristen Jozkowski, assistant professor of community health promotion in the College of Education and Health Professions, surveyed 185 students at Indiana University, where she earned a doctorate in health behavior. She wanted to examine how college students define consent and how they express and interpret consent in real-life sexual interactions.

Her study found that the use of nonverbal cues to interpret consent to sexual intercourse could lead to miscommunication and, in some cases, could result in unwanted sexual advances and sexual assault. She found significant differences in how men and women communicated their consent to intercourse with women using more verbal strategies and men using more non-verbal strategies. She found men also relied more on non-verbal indicators when interpreting their partner's consent and non-consent than women did.

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Low-Temperature Water Transition Identified

Feng Wang

Researchers at the University of Arkansas have identified that water, when chilled to a very low temperature, transforms into a new form of liquid.

Through a simulation performed in "supercooled" water, a research team led by chemist Feng "Seymour" Wang, confirmed a "liquid-liquid" phase transition

- Fran Hagstrom, $223,078, Arkansas Department of Workforce Education
- Daniel Lessner, $210,630, National Science Foundation
- Fred Limp, $135,000, Arkansas Natural and Cultural Resources Council

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at 207 Kelvins, or 87 degrees below zero on the Fahrenheit scale.

The properties of supercooled water are important for understanding basic processes during cryoprotection, which is the preservation of tissue or cells by liquid nitrogen so they can be thawed without damage, said Wang, an associate professor in the department of chemistry and biochemistry in the J. William Fulbright College of Arts and Sciences.

The findings were published online July 8 in the journal Proceedings of the National Academy of Sciences. Wang wrote the article, “Liquid–liquid transition in supercooled water suggested by microsecond simulations.” Research associates Yaping Li and Jicun Li assisted with the study.

Learn More

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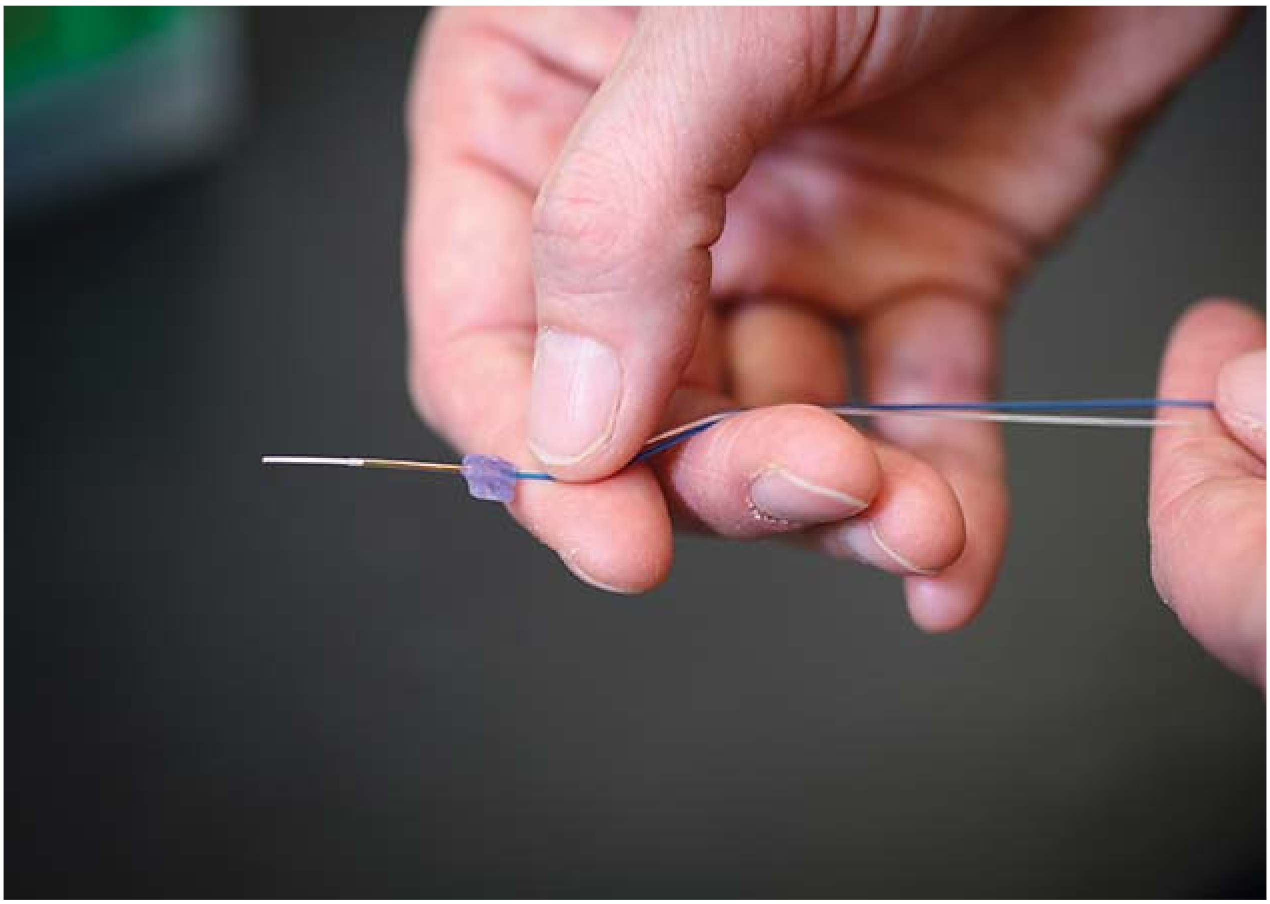
University of Arkansas

Research Frontiers

Probing for Answers Improving Sensors for Diabetics by Re-directing Macrophages

By Chris Branam



It's easy to measure glucose in a beaker.

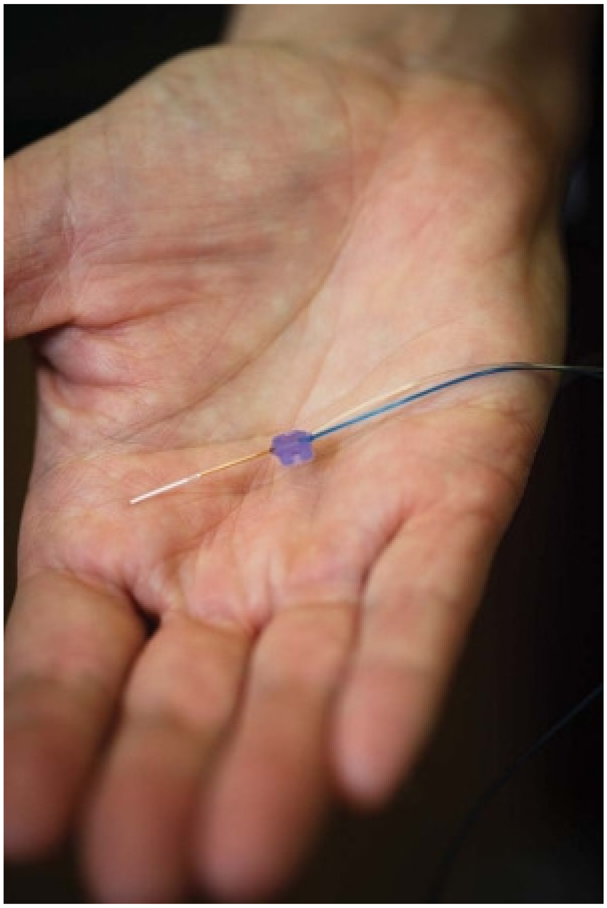
But the simple sugar is hard to quantify directly in the human body, which is why long-term glucose monitoring for people with type 1 and type 2 diabetes through implantable devices has proven to be extremely difficult. Leland Clark of Cincinnati Children's Hospital, considered the "Father of Biosensors," first suggested the use of electrodes for measurement of glucose in humans with diabetes in 1962. But a half-century later, diabetics still do not have ways to better manage their diabetes other than finger sticks or implanted sensors that have to be replaced every five to seven days.

The challenges scientists have faced in developing reliable implantable glucose sensors are two-fold: the sensors must deal with the foreign-body reaction, where a person's body attempts to wall off the implanted material from healthy tissue, and just as importantly, blood chemistry and tissue vary from person to person. After a week, these natural phenomena cause erratic glucose readings from sensor implants, said Julie Stenken, professor of chemistry and biochemistry.

"The whole foreign-body reaction drives a series of immune responses that then serve to encapsulate the sensor away from healthy tissue," Stenken said. "This sensor is measuring glucose in an encapsulated 'bag' around the sensor rather than being able to sense what is out in healthy tissue. That becomes an extremely dangerous situation clinically, because if you dose with insulin when you don't need to, the person can go into diabetic coma or eventually death due to an inaccurate reading from the sensor."

Stenken is a leading expert in the area of *in vivo* (in the body) collection of proteins known as cytokines using a technique called microdialysis sampling. Her aim is to understand the inflammatory response caused by cells called macrophages to implanted foreign materials. But first she must ask the question: How can we change the way these cells communicate with each other?

Research to Extend Lives



Big numbers illustrate the importance of Julie Stenken's work. An estimated 26 million Americans have diabetes, and another 79 million are experiencing symptoms of pre-diabetes, according to the American Diabetes Association. The association estimated the total annual cost of diabetes in the United States to be $218 billion in 2007, the last year figures were available. That total included direct medical costs and indirect costs such as disability, work loss and premature death.

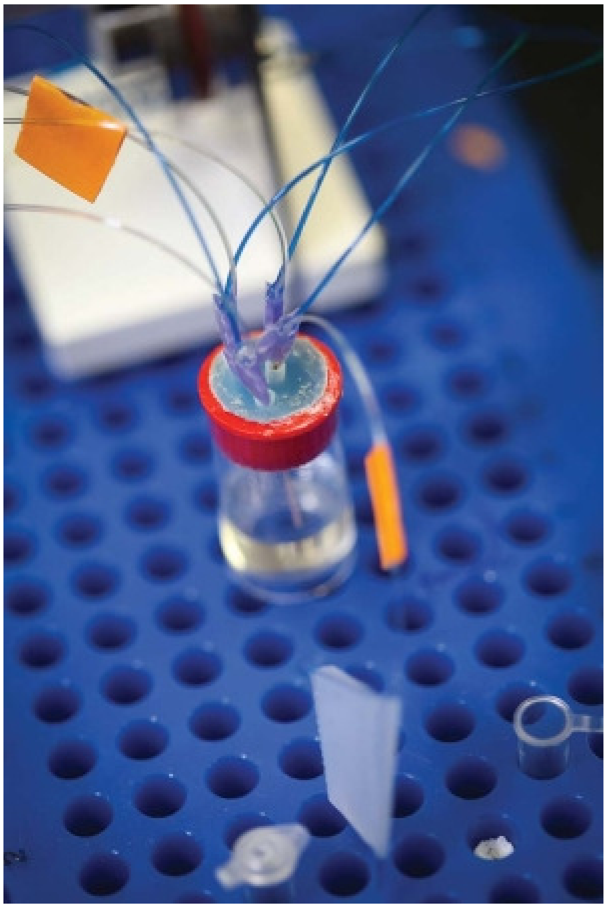
Even with the numbers of diabetics growing by an estimated 2 million a year, according to the association, only two companies are currently marketing implantable glucose sensors to American diabetics. A third discontinued its model in 2011. Type 1diabetes is a serious medical condition. Extending the implanted glucose sensor's lifetime is crucial to the future well-being of this large population, Stenken said.

"Current glucose sensors still have to be calibrated against a finger stick on a regular basis," Stenken said. "So if you had a glucose sensor that was better integrated into the body, where you could reduce the calibrations that you need — and have it last a longer period of time — people would be more compliant with their insulin doses. It would be very helpful in managing their disease."

Also, episodes of nocturnal hypoglycemia are of particular concern for diabetics who rely on glucose sensors. When blood glucose drops to low levels during sleep, the person experiences symptoms such as headache, fatigue or night sweats. Untreated nocturnal hypoglycemia can cause the sufferer to slip into a diabetic coma. Scientists are working to create a glucose sensor that would signal an alert that would remind the person to consume carbohydrate.

The Host Response

Understanding the underlying biochemistry that occurs at the site of an implanted biomaterial is important in a wide range of clinical contexts, from reconstructive surgery to implantable glucose sensors. Many of the problems that scientists have encountered in the development of implanted sensors into living things have been due to the lack of understanding of the host response to implanted materials, said Stenken, the Twenty-First Century Chair in Proteomics in the J. William Fulbright College of Arts and Sciences.



"In this whole process, the macrophage cells that are ultimately encapsulating this device communicate with each other through protein signals," Stenken said. "These messenger proteins, called cytokines, are part of a whole series of proteins that are involved in network responses within the immune system. We need to understand this communication process between all the cells so that we can direct the cells to the state where we want them to be."

This chemical signaling response to an artificial material within a tissue includes large cells known as macrophages. In an immune response, it is the job of the macrophage to destroy a foreign object, typically a virus or bacteria. The term is literally translated from Greek as "big eater." When the macrophages discover that they cannot destroy an object as large as a glucose sensor, they signal for fibroblast cells to lay down collagen, a group of proteins that form the main structural component of animal connective tissue. This "glue" eventually encapsulates an object, in this case a glucose sensor.

"There's an enormous interest in trying to redirect or bioengineer this whole process to improve outcomes," Stenken said. "These macrophages are very plastic. They have different states. We're trying to direct the macrophages to a certain type of cell, the M2. The M1 state is the classically activated macrophage where it is trying to destroy foreign material as quickly as possible. It's pro-inflammatory. The M2 state is considered to promote a wound-healing state."

To direct the macrophages, Stenken's research group uses a microdialysis probe that is placed under the skin of rats in order to mimic an implanted glucose sensor. The researchers, in a process unique to this group, then infuse different agents through the probe that are hypothesized to direct the macrophages into the M2, or healing, state.

"Once they are driven into the healing state, the question is, 'Do you see a longer lifetime for the implant?'" she said.

Stenken's work has drawn the attention of researchers across the country, including William M. Reichert, a distinguished professor of biomedical engineering at Duke University who has worked on biosensors.

"Julie has almost single handedly made a finicky microdialysis system work for the monitoring of wound healing," Reichert said. "I did some of this in the past but more or less gave up because of all of the experimental problems that she somehow overcomes. This can only be the mark of a careful and skilled experimentalist."

Federally Funded Research

In 2007, Stenken came to the U of A to accept an appointment as the inaugural holder of the Twenty-First Century Chair in Proteomics. The chair was endowed with a $1.5 million gift raised by the university's Campaign for the Twenty-First Century. She brought with her ongoing microdialysis research that included two grants totaling more than $1 million from the National Institutes of Health.

In addition to the current NIH grant, Stenken received a two-year, $375,000 grant from the national institutes to use the microdialysis probe to study cytokines in the brain. The Exploratory Developmental Research Grant (R21) will help to develop analytical chemistry methods to collect and detect cytokine proteins to allow for rapid translational medical treatments for humans. Cytokines as well as other neuropeptides are known to affect different human diseases related to the brain including, but not limited to, alcoholism, anxiety, appetite, depression, epilepsy, multiple sclerosis, pain, sleep, and various psychiatric disorders. These peptides and proteins are difficult to measure in the living brain.

"Cytokines are now considered the third-generation chemical communication system in the brain behind neurotransmitters and neuropeptides," Stenken said. "People have been very interested in cytokines in the brain because there are known receptors and they show up in many neurodegenerative diseases."

NIH R21 grants are meant to encourage high risk/high return research efforts. Stenken is enthusiastic about the possibilities.

"There are many biological areas that I know that these microdialysis probes will prove to be beneficial," she said. "I'm not afraid to learn new things in biology."

Stenken and Proteomics

Proteomics is the large-scale study of the structure and function of proteins. Julie Stenken is leading a research team that received a four-year, $1.3 million grant from the National Institutes of Health to study the "foreign body" response to implants.

Stenken is collaborating on the grant with Jeannine Durdik, professor of biological sciences and assistant dean for research in the Fulbright College of Arts and Sciences, and Liping Tang, professor of bioengineering at the University of Texas at Arlington.

In 2009, Stenken co-edited In Vivo Glucose Sensing with David D. Cunningham of Abbott Laboratories. The book, part of the Wiley Chemical Analysis series, is designed to provide state-of-the-art information on glucose monitoring to clinicians and medical educators.

Photos by Russell Cothren

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University of Arkansas Arkansas Newswire

Research: Genders Communicate Consent to Sex Differently

Professor suggests implications for sexual assault prevention efforts

Tuesday, July 02, 2013

Kristen Jozkowski

FAYETTEVILLE, Ark. – A University of Arkansas researcher's work on the way men and women communicate their consent to have sex could lead to improved sexual assault prevention programs on college campuses.

Kristen Jozkowski, assistant professor of community health promotion in the College of Education and Health Professions, surveyed 185 students at Indiana University, where she earned a doctorate in health behavior. She wanted to examine how college students define consent and how they express and interpret consent in real-life sexual interactions.

Her study found that the use of nonverbal cues to interpret consent to sexual intercourse could lead to miscommunication and, in some cases, could result in unwanted sexual advances and sexual assault. She found significant differences in how men and women communicated their consent to intercourse with women using more verbal strategies and men using more non-verbal strategies. She found men also relied more on non-verbal indicators when interpreting their partner's consent and non-consent than women did.

"The ways men and women look for cues to indicate consent and interpret them differs and this could potentially lead to unwanted sex," Jozkowski said. "We all talk in code."

For example, when she conducted interviews with college students, Jozkowski said, a male participant described how college students communicate in code. He indicated that he may ask a woman to come to his house and watch a movie. Because of the context of their relationship and the timing of the invitation, he may interpret that invitation as an invitation for sex. In a different context with potentially a different woman, he may just mean watching a movie.

Analyses of how participants actually communicated and interpreted consent suggested that many college students, despite defining consent as an explicit communication of agreement, often use consent signals that are less clear than providing explicit permission or saying yes, Jozkowski found. Sexual assault prevention education that addresses gender differences in consent communication may help men and women see the value in direct, verbal communication of consent, she said.

"They are saying something, but meaning something else, and they think the intended message is well understood given other contextual cues," Jozkowski said. "But what is really going on from our analyses is that men and women have disjunctive views of consent. Both think they understand each other but really the two (men and women) have different understandings of what these codes mean."

Many sexual assault prevention efforts focus on clear communication of consent as a way to reduce sexual assault but little research examines how heterosexual college students conceptualize sexual consent, she said. Most colleges and universities provide sexual assault prevention education to students but incident rates have not fallen over the past 50 years.

Jozkowski is lead author of "Gender Differences in Heterosexual College Students' Conceptualizations and Indicators of Sexual Consent: Implications for Contemporary Sexual Assault Prevention Education" scheduled to be published later this year in the *Journal of Sex Research* and "College Students and Sexual Consent: Unique Insights," also scheduled to be published next month in the *Journal of Sex Research* *(http://www.tandfonline.com/doi/full/10.1080/00224499.2012.700739#.UdGKtpze7e4)* and currently available online.

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University of Arkansas
Arkansas Newswire

University of Arkansas Researchers Identify Transformation in Low-Temperature Water

'Liquid-liquid' phase transition occurs at 87 degrees below zero

Wednesday, July 10, 2013

Feng Wang, University of Arkansas

Researchers at the University of Arkansas have identified that water, when chilled to a very low temperature, transforms into a new form of liquid.

Through a simulation performed in "supercooled" water, a research team led by chemist Feng "Seymour" Wang, confirmed a "liquid-liquid" phase transition at 207 Kelvins, or 87 degrees below zero on the Fahrenheit scale.

The properties of supercooled water are important for understanding basic processes during cryoprotection, which is the preservation of tissue or cells by liquid nitrogen so they can be thawed without damage, said Wang, an associate professor in the department of chemistry and biochemistry in the J. William Fulbright College of Arts and Sciences.

"On a microsecond time scale, the water did not actually form ice but it transformed into a new form of liquid," Wang said. "The study provides strong supporting evidence of the liquid-liquid phase transition and predicted a temperature of minimum density if water can be cooled well below its normal freezing temperature. Our study shows water will expand at a very low temperature even without forming ice."

The findings were published online July 8 in the journal *Proceedings of the National Academy of Sciences*. Wang wrote the article, "Liquid–liquid transition in supercooled water suggested by microsecond simulations." Research associates Yaping Li and Jicun Li assisted with the study.

The liquid–liquid phase transition in supercooled water has been used to explain many anomalous behaviors of water. Direct experimental verification of such a phase transition had not been accomplished, and theoretical studies from different simulations contradicted each other, Wang said.

The University of Arkansas research team investigated the liquid–liquid phase transition using a simulation model called Water potential from Adaptive Force Matching for Ice and Liquid (WAIL). While normal water is a high-density liquid, the low-density liquid emerged at lower temperatures, according to the simulation.

The research was supported by a National Science Foundation Faculty Early Career Development Award and by a startup grant from the U of A. The University of Arkansas High Performance Computing Center provided the main computational resource for the study.

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