

BIOPHYSICS NEWS

SCIENCE FEATURE

Sean McGarry, biophysics graduate student in the LaViolette lab, discusses his research interests.

My research interests lie in translating machine learning techniques into clinical practice in a manner that improves inter-user reliability. The LaViolette lab works in a subfield called rad-path (radiology-pathology) correlation. We align post-surgical tissue samples with in vivo clinical imaging and write pattern detection algorithms that predict histological characteristics noninvasively.

Many sources of variability outside of the parameters of interest can influence the output of a machine learning algorithm, particularly in magnetic resonance imaging. Scanner parameters, coils, and field strength can create subtle signal differences that make an algorithm trained on one dataset difficult to generalize to a dataset acquired under different circumstances. Human error and ground-truth variability as well as post-processing decisions made by the investigator can add further error.

My research has evolved to focus on quantifying the effects of these sources of variability on the generalizability of machine learning algorithms. The LaViolette lab acquired a dataset of whole mount prostate slides annotated by five pathologists, and we used this dataset to demonstrate that inter-observer variability can have a substantial effect on the predictive power of a downstream machine learning algorithm. We compiled a dataset of diffusion fits from 13 institutions and examined the effects of post-processing decisions on the perceived diagnostic utility of each contrast with respect to what currently is used clinically. We hope that the outcome of this research will be a set of standards and best practices for other investigators creating biomarkers with rad-path datasets such that algorithms trained at MCW can seamlessly be utilized by any investigator at any institution worldwide to create biomarkers.

SAVE THE DATE

SfRBM Regional & MCW Redox Biology Symposium

The fifth annual SfRBM Regional Redox Symposium will be hosted by the MCW Redox Biology Program on June 26-27, 2020. The symposium will consist of two days of state-of-the-art research talks, both invited and chosen from submitted abstracts.

In addition, a pre-symposium MCW Regional Redox Workshop will take place on June 25, 2020, and will include a morning of didactic introduction to redox biology, focusing on the biological chemistry of reactive species and how to detect them, and an afternoon of hands-on practical experience.

Featured topics include immunology & inflammation, metabolomics & metabolism,

epigenetics, and redox systems.

Featured speakers:

- Ines Batinic-Haberle, PhD (Duke)
- Eduardo Chini, MD, PhD (Mayo Clinic)
- Victor Darley-Usmar, PhD (UAB)
- Cristina M. Furdul, PhD (Wake Forest)
- David Harrison, MD (Vanderbilt)
- Melissa Teoh-Fitzgerald, PhD (UNMC)
- Ming Xian, PhD (Washington State)

Symposium chairs:

- Neil Hogg, PhD
- Jeannette Vasquez Vivar, PhD

Visit the [SfRBM website](#) for additional details.

SEMINAR SERIES

Our Spring 2020 Graduate Seminar Series takes place most Fridays throughout the semester, from 9:30–10:30 am. Please join us!

Jan 17 | Rodney Willoughby, MD (MCW), Gaseous microintoxication by invasive bacteria

Jan 24 | Sarah Erickson-Bhatt, PhD (Marquette), Bioimaging of cancer

Jan 31 | Sean McGarry (MCW), Prostate cancer detection with multi-parametric MRI

Feb 14 | Jon M. Fukuto, PhD (Sonoma State), The chemical biology of hydropersulfides: Possible cellular protecting functions

Feb 21 | John Paul SanGiovanni, ScD (Univ Arizona), Carotenoids in retinal health and disease

Feb 28 | Richard Mett, PhD (UWM), Dielectric loop-gap resonators and multichannel sample tubes for X-band EPR spectroscopy of small aqueous samples

Mar 6 | Amanda Buchberger, PhD (MCW), Development and application of multi-faceted quantitative and qualitative mass spectrometry techniques for biomolecules

Mar 13 | Matthew Budde, PhD (MCW), Translational MRI in spinal cord injury: Promise and hurdles

Mar 27 | Ali Bakhshinejad, PhD (VasoGenosis), AI in diagnostic imaging

Apr 3 | Songi Han, PhD (UC Santa Barbara), Study of protein structure and interaction via the hydration water layer

Apr 10 | Xiao Chen, PhD (MCW), Potential role of vitamin A in graft-versus-host disease

Apr 17 | Balaraman Kalyanaraman, PhD (MCW), From Parkinson's disease to cancer and back to PD: Repurposing of mitochondria-targeted agents

DEPARTMENT NEWS

Welcome

- Patrick Brennan (graduate student, Lerch lab)
- Brooke Greiner (graduate student, Greenberg lab)

Farewell

- Zachary Boyd (graduate student, Paulson lab)
- Aleksandra Grzelakowska (postdoctoral fellow, Zielonka lab)
- Allison Kahlke (research technologist, Vasquez Vivar lab)

Congratulations

- Zachary Boyd: Received his MS
- Guangyu Chen & Shi-Jiang Li: Published a [paper](#) in PLoS One
- Gang Cheng, Jacek Zielonka, Alex Garces, Donna McAllister, & Balaraman Kalyanaraman: Published a [paper](#) in *Free Radical Biology and Medicine*
- Jimmy Feix: Published a [paper](#) in *Biophysical Journal*
- Balaraman Kalyanaraman: Published a [paper](#) in *Redox Biology* & a [paper](#) in *Journal of Biological Chemistry*
- Candice Klug & Christopher Kristich: Received a \$1.355M new [R01](#) from NIH/NIGMS
- Janet Pradarelli: Promoted to financial specialist
- Jeannette Vasquez Vivar: Published a [paper](#) in *Redox Biology*

Years of Service

Five Biophysics employees were honored for their years of service to MCW. Thank you for your commitment and hard work!

- Ted Camenisch, engineer IV (40 yrs) (*top*)
- Gang Chen, research scientist II (10 yrs)
- Gang Cheng, research scientist II (10 yrs)
- Donna McAllister, research associate (40 yrs) (*middle*)
- Jane Thelaner, admin. associate (40 yrs) (*bottom*)

Outstanding Educators

The Graduate School of Biomedical Sciences congratulated Outstanding Graduate School Educator pin recipients; among them are the following Biophysics graduate faculty. The pins are awarded annually to honor faculty who have made a significant contribution to graduate education.

- Jeffrey Binder, MD
- Neil Hogg, PhD
- Candice Klug, PhD
- Kathleen Schmainda, PhD
- Jeannette Vasquez Vivar, PhD

Also, **Candice Klug** received the Dean's Choice Outstanding Graduate School Educator award for 2018-2019.

Thanks to the Biophysics personnel who participated in department events--attended the holiday party, purchased gifts for the Friendship Inc. giving tree (*top left*), made cookies & wore holiday apparel (*top right*), made groundhog brownies, and attended the Packer party (*bottom right*)! Also, thanks to Janet Pradarelli & Jane Thelaner for organizing these events!



Biophysics Personnel:
**See you on
Souper Tuesday!**
Check your email
for details.



RECIPE

Glazed Salmon

Serves 4

Ingredients

- 1 teaspoon light brown sugar
- 1/2 teaspoon kosher salt
- 1/2 teaspoon cornstarch
- 4 center-cut skin-on salmon fillets (6-8 oz each)*
- Ground black pepper
- 1 teaspoon vegetable oil
- 1 recipe sherry glaze (see below)

Sherry Glaze

- 3 tablespoons brown sugar
- 2 tablespoons mirin
- 2 tablespoons soy sauce
- 1 tablespoon sherry vinegar
- 1 tablespoon water
- 1 tablespoon coarse ground mustard
- 1 teaspoon cornstarch
- 1/2 teaspoon red pepper flakes

Directions

1. Adjust oven rack to middle position and heat oven to 350°F.
2. Prepare sherry glaze: Mix all ingredients in a saucepan at medium heat; simmer for 2-3 min until mixture has thickened but not congealed. Turn off heat; cover.
3. Pat salmon dry with paper towels and season with pepper. Combine brown sugar, salt, and cornstarch in small bowl. Sprinkle brown sugar mixture evenly over the flesh side of the salmon, rubbing to distribute.
4. Heat oil in 12-inch (ovensafe) nonstick skillet** over medium-high heat until just smoking. Place salmon, flesh side down, in skillet and cook until well browned, about 1 min. Using tongs, carefully flip salmon and cook on skin side for 1 min.
5. Remove skillet from heat and spoon glaze evenly over fillets. Transfer skillet** to oven.
6. Cook until center of thickest part of fillets registers 125°F on instant-read thermometer and is still translucent when cut into with a paring knife, 7-10 min. Transfer fillets to a platter or individual plates and serve.

*Use fillets of similar thickness so they cook at the same rate. Buy a 1 1/2- to 2-lb center-cut fillet and cut it into 4 pieces.

**If your skillet is not ovensafe, sear the salmon as directed in step 4. Then, transfer it to a rimmed baking sheet, glaze it, and bake it as directed in step 6.

Submitted by Jeannette Vasquez Vivar.

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BIPHYSICS NEWS

SCIENCE FEATURE

Repurposing a mitochondria-targeted molecule from cancer to COVID-19-related research by Balaraman Kalyanarman, PhD, professor & chair of biophysics; associate director of basic research, Center for Disease Prevention Research

In early April, an NCI program director asked Dr. Ming You (Pharmacology/director of Center for Disease Prevention Research [CDPR]) if he was interested in applying for a COVID-19-related administrative supplement to an existing NCI-funded grant. Ming and I are co-PIs of an existing grant, "Chemoprevention of lung cancer by targeting lonidamine to mitochondria," so he asked my opinion. My first reaction was, *Is it worth my time?* As the national health crisis escalated, it quickly became apparent that as NIH-funded researchers, it was our moment to unite and use our collective expertise in defeating this deadly virus. In order to best address programmatic needs to enhance our understanding of the mechanism of action of this novel virus and potentially enable new, future drug treatment modalities for COVID-19 patients, Ming and I convened a group comprising Drs. Jimmy Feix and Jacek Zielonka (Biophysics) and Dr. Charley Meyers (Pharmacology/associate director of CDPR). Based on a publication

reporting the antibacterial properties of mitochondria-targeted agents, we decided to investigate mito-lonidamine, developed by Dr. Micael Hardy (Aix-Marseille Université), as a therapeutic agent to mitigate antibiotic-resistant bacterial infections in COVID-19 patients. Jimmy's expertise in antibacterial research, coupled with the insightful contributions from Jacek and Charley as well as Ming's years of experience in mice models of lung cancer and our recent publication in *Nature Communications* ([Cheng G et al. Nat Commun. 2019;10\(1\):2205](#)) resulted in the submission of a supplemental proposal, "Role of mitochondria-targeted lonidamine to mitigate antibiotic-resistant bacteria infections in patients with COVID-19 disease," which currently is in review. Regardless of the outcome, I found this to be a very satisfying effort! I am thankful for the CDPR and Biophysics staff and for Ming's persistence. Who knows? This may become a full-fledged R01! Stay tuned!

BIPHYSICS GRAD SCHOOL COURSES

Going Virtual & Reimagining the Seminar Series

Following Governor Evers' Safer-at-Home order and MCW directives, the Biophysics Graduate Program courses moved to an online format. This affected the Functional MRI Contrast Mechanisms and Applications course directed by Christopher Pawela, PhD; MRI Journal Club course, directed by Peter LaViolette, PhD; and Seminar course, directed by Candice Klug, PhD. The courses taught by Drs. Pawela and LaViolette finished out the semester via Webex. The Seminars course, for which students are required to attend in-person presentations by Biophysics Graduate Seminar Series speakers, had to be somewhat reimagined, as the seminar series was

canceled with five seminars remaining.

To complete the Seminar course, students were given the option of substituting a previously recorded Biophysics seminar or comparable MCW seminar of interest; a previously attended, comparable seminar from an MCW department other than Biophysics; an MCW dissertation defense or seminar of interest, attended virtually; or an online talk of scientific interest, such as a Ted talk, NIH talk, YouTube talk, or university lecture. According to Dr. Klug, the students readily adapted and enjoyed finding alternative content that was meaningful to their research.

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BIPHYSICS RESPONSE

Biophysics responded to the COVID-19 pandemic in line with guidance from MCW and the State of Wisconsin. One of its first decisions was to cancel the remainder of the spring Graduate Seminar Series to limit gathering size. Similarly, the Redox Biology Program, working with the Society for Redox Biology and Medicine, postponed its SfrBM Regional MCW Redox Biology Symposium.

Shortly thereafter, all MCW employees able to work remotely were mandated to do so, and labs were put into hibernation. One lab conducting critical ongoing experiments was granted permission to continue them. Biophysics graduate courses, including dissertation defenses, shifted to an online platform, as did lab group, faculty, and staff meetings.

Amid continuing uncertainty in this new working and learning environment, Balaraman Kalyanarman, PhD, encouraged Biophysics personnel to control what was within their grasp: finish an old paper; write a review; or find COVID-19-related RFAs and, based on individual strengths and expertise, determine how to contribute to understanding the SARS-CoV-2 mechanism of action. He also encouraged maintaining a good work/life balance and exercise schedule; eating healthy foods; and being kind to each other, particularly essential employees.

In early May, Biophysics labs began the initial, voluntary phase of ramp up, which comes with constraints: the PI and one lab member are allowed in the lab and must practice social distancing and follow all MCW safety and decontamination precautions. Experiments must be minimal and able to be completed within the time allotted, and data analyses must be conducted at home.

We are in a recovery mode. As institutional guidance evolves, Biophysics will continue to ramp up lab operations with the goal of maintaining a safe and productive work environment.

DEPARTMENT NEWS

Welcome

- Roger Johnson (associate professor; Director of Programmatic Grants and Strategic Partnership Development, Cancer Center)
- Kathryn Schultz (research scientist, Klug lab) [returned in January]

Congratulations

- Gang Chen, Doug Ward, & Shi-Jiang Li published a [paper](#) in *American Journal of Geriatric Psychiatry*.
- Gang Cheng, Jacek Zielonka, Kathleen Schmainda, & Balaraman Kalyanaraman published a [paper](#) in *Cell Communication and Signaling*.
- Neil Hogg published a [paper](#) in *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*.
- Balaraman Kalyanaraman published a [paper](#) in *Environmental Science & Technology*.
- Balaraman Kalyanaraman & Jacek Zielonka published a [paper](#) in *Journal of Biological Chemistry*.
- Kathleen Schmainda published a [paper](#) in *American Journal of Neuroradiology* and received a UG3 (subcontract from Dignity Health, PI: Quarles)
- Karol Subczynski published a [paper](#) in *Cell Biochemistry and Biophysics*.
- Jeannette Vasquez Vivar published a [paper](#) in *Free Radical Research Biology and Medicine* and received an R01 (subcontract from Wayne State University, PI: Tan).

Dissertation Defense Announcement

“Predictive Modeling of Prostate Cancer Biomarkers with Magnetic Resonance Imaging” presented by Sean McGarry (advisor: Peter LaViolette, MS, PhD) on Tuesday, June 9, 2020, at 10 am; [public viewing online](#).

While Safer-at-Home

On short notice, we were asked to adapt to a nonstandard way of life. The challenges are many and the news often is dire, yet our time while safer-at-home has been beneficial. Biophysics personnel have delved into various activities, both personal and professional. The commute to/from work and morning rush have been replaced with family meals and time together. Dads have become jokesters. Dog lovers have become first-time foster families and new dog owners. Gardeners have found a renewed connection with the flora and fauna in their yards. Students have completed experiments, finished research, and on occasion given themselves permission to “underachieve.” Professors have found time to publish papers, help students, and work on grants. Many of us have dabbled in cooking, photography, music, reading, or crafts, and some have become teachers, caretakers to parents, friendly voices on the phone, or volunteers for COVID-19-related efforts; others have taken on home projects, enjoyed nature walks, ridden bikes, or allowed themselves to relax. Though we are anxious to resume our lives, we have felt the importance of our time and have learned that we should rethink what we had considered normal.

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Given the enthusiasm for the virtual format, as well as the uncertainty regarding the duration of social distancing guidance, the Biophysics faculty discussed taking the fall 2020 Biophysics Graduate Seminar Series, which is run by Jeannette Vasquez Vivar, PhD, entirely virtual.

Outside speakers, including those originally scheduled to speak during the spring 2020 series, will be invited for talks and visits like before, only in a virtual format. Going virtual will open the series in the future to any speaker regardless of their location, including international speakers, and potentially allows for a much broader audience. Also, Dr. Klug is considering how and whether to incorporate some talks selected by the students into the syllabus for credit, as was done this spring semester. All in all, these changes are expected to greatly improve the course.

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RECIPES

Chocolate Frappé

1 serving

Ingredients

- ½ cup dairy or non-dairy milk
- 2 tablespoons unsweetened Dutch-processed cocoa powder
- 1 tablespoon sugar
- 3 ice cubes
- Whipped cream (optional)
- Chocolate shavings (optional)

Directions

1. Put milk, cocoa, sugar, and ice cubes in a cocktail shaker.
2. Shake for 30-45 seconds.
3. Remove the lid from the shaker and pour the frappé into a chilled glass. (You can include any pieces of ice that remain or strain them out.)
4. Spoon any mousse (foam) left in the shaker on top of the frappé.
5. If desired, garnish with whipped cream and chocolate shavings.



Spiced Glazed Nuts & Pretzel Mix

~4 cups

Ingredients

- 2 cups mixed raw nuts
- 1 tablespoon butter, melted
- 3 tablespoons dark brown sugar
- ½ teaspoon ground cinnamon
- ¾ teaspoon cayenne or red pepper
- 1 ½ tablespoons maple syrup
- 1 teaspoon flaky sea (or kosher) salt
- 2 cups small pretzel twists

Directions

1. Spread nuts on a baking sheet & roast at 350°F for 20 min, stirring once.
2. In medium bowl, mix melted butter, brown sugar, cinnamon, pepper, & maple syrup.
3. Add warm nuts and stir until the nuts are completely coated.
4. Mix in pretzels, spread mixture back on the baking sheet, and return to the oven for 12-18 min, stirring a few times.
5. Remove from oven & cool completely, separating the mixture as it cools.

Obtained from David Lebovitz's [Drinking French](#) & [blog](#).

BIOPHYSICS NEWS

SCIENCE FEATURE

Balaraman Kalyanaraman, PhD, professor & chair of biophysics; associate director of basic research, Center for Disease Prevention Research

My review article, titled *Do free radical NETWORK and oxidative stress disparities in African Americans enhance their vulnerability to SARS-CoV-2 infection and COVID-19 severity?*, was recently published in *Redox Biology*. Following is the abstract for the review article:

This review focuses on the hypothetical mechanisms for enhanced vulnerability of African Americans to SARS-CoV-2 infection, COVID-19 severity, and increased deaths. A disproportionately higher number of African Americans are afflicted with autoimmune and inflammatory diseases (e.g., diabetes, hypertension, obesity), and SARS-CoV-2 has helped expose these health disparities. Several factors including socioeconomic status, inferior health care, and work circumstances contribute to these disparities. Identifying potential inflammatory biomarkers and decreasing basal levels in high-risk individuals with comorbidities through preventive measures is critical. Immune cells, particularly neutrophils, protect us against

pathogens (bacteria, fungi, and viruses) through increased generation of free radicals or oxidants and neutrophil extracellular traps (NETs) that ensnare pathogens, killing them extracellularly. However, continued generation of NETs coupled with the lack of prompt removal pose danger to host cells. NET levels are increased during pro-inflammatory diseases. COVID-19 patients exhibit elevated NET levels, depending upon disease severity. Conceivably, high-risk individuals with elevated basal NET levels would exhibit hyper-inflammation when infected with SARS-CoV-2, amplifying disease severity and deaths. Drugs inhibiting oxidant formation and vitamin supplements decreased NET formation in mice models of inflammation. Thus, it is conceivable that preventive treatments lowering NET levels and inflammation in high-risk individuals could mitigate SARS-CoV-2-induced complications and decrease mortality.

The [full article](#) is available on the *Redox Biology* website.

WORKING TOWARD ANTIRACISM

In light of the global protests sparked by the death of George Floyd, and the intensified focus on the need for anti-racism, MCW has declared its commitment to becoming an antiracist organization.

Here are some small things you can do to begin learning about racism, anti-racism, and how to enact change:

- Read the [MCW Common Read book](#), *How to Be an Antiracist*, by Ibram X. Kendi and participate in the related book discussions. Biophysics has purchased two copies of this book; please contact jthelane@mcw.edu to borrow a copy.
- Visit the [Office of Diversity and Inclusion](#)

[website](#), which offers a plethora of information to guide learning.

- Participate in MCW *Community Listening Circles on Racism* and in Office of Diversity and Inclusion *Anti-Racist Learning and Growth* sessions when they are offered. Watch InfoScope and your email for information on upcoming sessions.

Some of this information may be new or uncomfortable, but approach it with an open mind and heart. Our missions, including the Biophysics mission of quality in research and graduate and post-doctoral training, will be better achieved through antiracism, equity, diversity, and inclusion.

SEMINAR SERIES

Our **Fall 2020 Graduate Seminar Series** takes place **VIRTUALLY most Fridays** throughout the semester, from **9:30–10:30 a.m. unless otherwise noted**. Please visit the [Biophysics Events page](#) to join us!

Sept. 11 | Song-I Han, PhD (UCSB), Study of protein structure and interaction via the hydration water layer [10:30 a.m. start time]

Sept. 18 | Neil Hogg, PhD (MCW), Nitric oxide and SARS-CoV-2: Antiviral effects of NO

Sept. 25 | Ethan Duwell (MCW), Albinism, a window on the effects of aberrant retinotopy in vision

Oct. 02 | Aashish Manglik, MD, PhD (UCSF), Building keys to understand the lock: engineering conformation-specific antibodies to probe transmembrane signaling

Oct. 09 | Jason Sidabras, PhD (MPIEC), Application-specific microwave resonator development: Addressing the challenges of modern EPR [10:30 a.m. start time]

Oct. 23 | X. Allen Li, PhD, DABMP, FAAPM (MCW), Delta radiomics for cancer treatment response assessment

Oct. 30 | Ali Bakhshinejad, PhD (VasoGenosis), AI in diagnostic imaging

Nov. 06 | John LaDisa, Jr., PhD (Marquette), Image-based experimental and computational approaches to studying vascular adaptation in response to mechanical stimuli

Nov. 13 | Matthew Budde, PhD (MCW), Translational MRI in spinal cord injury: Promise and hurdles

Nov. 20 | Nicole Lohr, MD, PhD, FACC (MCW), Unraveling the role of 670 nm energy on intracellular NO and oxidative stress

Dec. 04 | Adam Greenberg, PhD (MCW & Marquette), Uncovering the computations mediating attentional control in posterior parietal cortex

Dec. 11 | Michael Davies, DPhil (UCPH), Oxidative damage to long-lived proteins: Biomarkers of damage and contributors to disease

DEPARTMENT NEWS

Welcome

- Anjana Adhikari (research technologist, Lerch lab)
- Savannah Duenweg (graduate student, LaViolette lab)

Farewell

- Sean McGarry (graduate student, LaViolette lab)

Congratulations

- Mona Al-Gizawiy & Kathleen Schmainda published a [paper](#) in *Oncotarget*.
- Alex Helfand received his PhD.
- Neil Hogg and Scott Terhune received the Center for Immunology's COVID-19 Research Award.
- Balaraman Kalyanaraman published a [paper](#) in *Redox Biology*, [another paper](#) in *Redox Biology*, and a [paper](#) in *Cell Biochemistry and Biophysics*.
- Candice Klug published a [paper](#) in the *Journal of Biological Chemistry*.
- Michael Lerch published a [paper](#) in *Science*.
- Sean McGarry received his PhD.
- Melissa Prah & Kathleen Schmainda published a [paper](#) in *Tomography* and a [paper](#) in *Neuro-Oncology*.
- Melissa Prah, Kathleen Schmainda, & Cathy Marszalkowski published a [paper](#) in *International Journal of Radiation Oncology*Biological*Physics*.
- Kathleen Schmainda published a [paper](#) in *Neuro-Oncology*.
- Karol Subczynski published a [paper](#) in *Nutrients* and a [paper](#) in *Cell Biochemistry and Biophysics*.
- Jacek Zielonka & Balaraman Kalyanaraman published a [paper](#) in *Redox Biology* and a [paper](#) in *Free Radical Biology and Medicine*.

Dr. Schmainda Inducted as ISMRM Fellow

Kathleen Schmainda, PhD, was inducted as an International Society for Magnetic Resonance in Medicine (ISMRM) fellow at the annual meeting, held virtually Aug. 8-14, 2020. She joins previous ISMRM fellows associated with Biophysics, including James S. Hyde (1996), Andrzej Jesmanowicz (2002), Peter A. Bandettini (2015), and Eric Wong (2015). ISMRM fellows are selected based on their contributions and impact to the field of magnetic resonance in medicine, as well as their role in ISMRM.

The essence of the award is captured by the [recently published paper](#) of which Dr. Schmainda is the senior author. The paper sets forth national recommendations regarding the best way to collect perfusion MRI data for brain tumors---it is based in large part on Dr. Schmainda's studies from the past 20 years. In short, the data collection method used by the Schmainda group is now THE national standard.

Dr. Kalyanaraman Receives MCW Distinguished Service Award

Balaraman Kalyanaraman, PhD, is one of three 2020 recipients of MCW's Distinguished Service Award, the institution's highest faculty and staff honor.

Dr. Kalyanaraman has served MCW through outstanding scholarship and leadership for nearly 40 years. He is an internationally recognized expert on free radical biochemistry and biology and has developed novel approaches that contributed to the growth and development of this scientific field and has applied these methods to advance understanding of the role of mitochondria in cancer, Parkinson's disease, cardiac injury, neuronal injury, and vascular biology. His lab's findings in these studies have significant therapeutic implications. More than 50 research scientists, postdoctoral fellows, graduate students, and undergraduate students have benefited from Dr. Kalyanaraman's mentorship, as have hundreds of graduate and medical students from his teaching activities. Dr. Kalyanaraman has authored over 400 research articles and more than 60 reviews and book chapters, and holds 8 patents. The NIH has supported his research continuously for 35 years.

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Click to Register



Nov. 3 General Election

RECIPE

Summer Squash Pizza



Servings: 4-8

Ingredients

- 1 tablespoon olive oil, plus more for fingertips
- 1 recipe pizza dough [see below*]
- 2 1/2 pounds zucchini or other summer squash, trimmed (~5 small/medium or 3 large)
- 1 1/2 teaspoons fine sea salt
- 2 cups (8 oz) coarsely grated Gruyère cheese
- 2-3 tablespoons plain breadcrumbs

Directions

Heat oven to 485°F with a rack in the center. Brush a 13×18-inch rimmed half-sheet pan with olive oil. Use oiled fingertips to pull, stretch, nudge, and press the dough evenly across the bottom of the pan.

Grate the zucchini. In a large bowl, toss together the zucchini and salt; let stand for 20 to 30 min (or more). Use a clean dishtowel to squeeze water from zucchini. Toss the zucchini with the Gruyère shreds, being sure to break up any clumps of zucchini. Salt to taste, and add any other seasonings desired.

Spread the zucchini mixture over the dough, to the edges of the pan and pile it a bit thicker at the edges, where it will brown first. Sprinkle messily with the bread crumbs.

Bake for 20 to 25 min, until golden. Remove from oven and cut into squares.

*Jim Lahey's Basic Pizza Dough (modified)

- 2 cups minus 1 tablespoon all purpose flour
 - 1 1/4 teaspoons instant or active dry yeast
 - Heaped 1/4 teaspoon fine sea salt
 - 2/3 cup room temperature water
- Stir together the flour, yeast, and salt. Add the water and mix until well blended, about 30 sec. Cover the bowl and let sit at room temperature until the dough has more than doubled in volume, ~2 h.

Recipe obtained from [Smitten Kitchen](#).

BIOPHYSICS NEWS

REFLECTING ON 2020

The year 2020 has been devastating to each of us in different ways—physically, mentally, and socially—and some of us have been disproportionately and unfairly impacted. Forever changed are our realities, relationships, perceptions, needs, identities... the list goes on. Some of these outcomes are negative and have profoundly harmed us and/or those we love, some will change again with time, and some come with hidden benefits; these are not necessarily discordant.

Looking back, 2020 is both the year that never was and, arguably, the most important year of some of our lives. The culmination of events across the spectrum brought to boil social tensions that have long been simmering, while simultaneously allowing us the time and space to sit with and consider their origins and implications. A lot can be learned from this year if we choose to look and listen, and what we gain or lose is uniquely ours.

Events of this year have forced change on so many levels, and we have been left with a nagging uneasiness. Rather than fighting the inevitable and focusing solely on what could or should

have been, why not look forward and try to grasp the tangible?

Do not let 2020 be a lesson in passivity; consider it inspirational to enacting the changes you wish to see. Start small and grow from there; begin within your household, department, or neighborhood. You may find solace in proactivity; you also may pause if you become overwhelmed.

If each of us performed small acts of kindness, we may inspire those around us. Consider what we could accomplish if we work together and build each other up. Sam Cooke's words seem relevant to this sentiment: "There have been times that I thought I couldn't last for long, but now I think I'm able to carry on. It's been a long, a long time coming, but I know a change is gonna come."

More than one social media platform has referred to this year as a dumpster fire, but if we take what we have learned (the negatives with the positives) and use it to help one another, maybe—like the phoenix—we will rise from the ashes, empowered with knowledge and filled with ambition in 2021.

CONGRATS!

Dr. Candice S. Klug named James S. Hyde Professor of Biophysics

Candice S. Klug, PhD, was named the James S. Hyde Professor of Biophysics effective Oct. 1.

This endowment was created in recognition of Dr. Jim Hyde's work to educate, inspire, and shape the careers of generations of scientists and inventors, as well as his achievements as a pioneer and innovator in the application of EPR instrumentation and MR technologies. Dr. Klug will be an outstanding steward of this endowment. Her re-

markable success in obtaining extramural funding in EPR will help move techniques developed at the EPR Center into new and emerging areas of structural biology.

An endowed professorship is one of MCW's permanent and sustaining assets and, as such, it is one of MCW's most important faculty honors. Please join me in congratulating Candice on this exciting achievement!

[Read the full announcement.](#)

MUST WATCH

In parallel with MCW Professionalism Week, MCW Basic Sciences screened the documentary, [Picture a Scientist](#). The film examines the systemic gender and racial discrimination, as well as underrepresentation, experienced by women in science through the firsthand accounts of three female scientists (chemist Raychelle Burks, biologist Nancy Hopkins, and geologist Jane Willenbring) in different fields and stages of their careers. Intertwined are supporting data and the perspectives of social scientists, neuroscientists, and psychologists, who offer ways science can be made more diverse, equitable, and accessible.

Women make up less than one-third of all working scientists; this number is even smaller for women of color. Of the 616 Nobel laureates in science from 1901–2019, only 19 were women and one was a woman of color.

Picture a Scientist shows us that although a good pipeline exists to get girls and women into STEM fields, harassment and discrimination cause many to leave these fields. This phenomenon, known as the "leaky pipeline," is significant because, as Hopkins says, "if you don't have women, you've lost half of the best people. Can we really afford to lose those top scientists?"

Many choose to ignore gender discrimination in science or to believe it is no longer a problem; however, as discussed in the film, experimental evidence shows unconscious [bias is pervasive in science](#). Psychologist Mahzarin Banaji poses the question, "How many great discoveries have just been lost to us because we didn't have the eyes to see?"

This film is simultaneously heartbreaking and inspiring; it is highly recommended. Thank you to Dr. Michelle Riehle, assistant professor of microbiology and immunology, for organizing the screening.

DEPARTMENT NEWS

Welcome

- Nick Cina (IDP student rotating through Klug Lab, Nov. 2 - Dec. 11)
- Priscilla Kyi (IDP student rotating through Hogg Lab, Nov. 2 - Dec. 11)
- Jillian Ward (research technologist I, Vasquez Vivar lab)

Farewell

- Hai Tran (IDP student rotated through Hogg Lab, Sept. 21 - Oct. 30)

Congratulations

- Gang Cheng & Balaraman Kalyanaraman published a [paper](#) in *Scientific Reports*.
- Gang Cheng, Jacek Zielonka, Monika Zielonka, & Balaraman Kalyanaraman published a [paper](#) in *Cancer Treatment and Research Communications*.
- Jimmy Feix was recognized for 35 years of faculty service to MCW & published a [paper](#) in *Scientific Reports*.
- Neil Hogg published a [paper](#) in *Nitric Oxide*.
- Balaraman Kalyanaraman was recognized for 35 years of faculty service to MCW.
- Candice Klug, Peter LaViolette, Michael Lerch, and Eric Paulson each received an Outstanding Graduate School Educator recognition pin for 2019-2020.
- Natalia Stein & Karol Subczynski published a [paper](#) in *Applied Magnetic Resonance*.
- Jacek Zielonka was promoted to director of the MCW Cancer Center Redox and Bioenergetics Shared Resource, received an AHW Limited Needs Award, & published a [paper](#) in *Blood Advances*.
- Jacek Zielonka & Balaraman Kalyanaraman published a [paper](#) in *Scientific Reports* & a [paper](#) in *Frontiers in Chemistry*.

MCW Community Giving Campaign

For the MCW Community Giving Campaign this year, Janet Pradarelli organized a “Who’s Who” game, wherein she collected childhood photos of departmental personnel and of President Raymond and Dean Kerschner. In return for a small donation to United Way, participants had the opportunity to guess which photograph belonged to which individual. Thank you, Janet, for your efforts in leading Biophysics’s participation in this year’s MCW’s Community Giving Campaign, and for putting this activity together! Playing the game was sometimes challenging, and it was a fun (and adorable) break in the day. Also, thank you to all of our colleagues who participated!

Donations to United Way are particularly important during these troubling times and will help members of our community who have few other resources. Please consider contributing to United Way’s [Holiday Giving Tree](#) to purchase a gift for a community member in need.

Virtual Research Week: February 22–26, 2021

The Office of Research’s Virtual Research Week will include short talks; resource sessions; and live, virtual poster presentations. The [call for abstracts is open](#) now through January 11.

Attn.: Biophysics Personnel

The annual Biophysics holiday party will be held virtually this year. Watch your email for additional details!

Biophysics News is a quarterly MCW departmental newsletter aimed at enhancing departmental engagement through information and good news sharing. Do you have information you’d like to share—news, a photo, a recipe? [Send it to Lydia](#).

RECIPE

Pumpkin Pie Crunch



Ingredients

- 1 (16 oz) can solid pack pumpkin
- 1 (12 oz) can evaporated milk
- 3 large eggs
- 1 ½ cups sugar
- 4 teaspoons pumpkin pie spice
- ½ teaspoon salt
- ½ package yellow cake mix
- 1 cup chopped pecans
- 1 cup butter or margarine, melted
- whipped topping

Directions

1. Preheat oven to 350°F.
2. Grease a 13×9×12-inch pan.
3. Combine pumpkin, evaporated milk, eggs, sugar, pumpkin pie spice, and salt in a large bowl.
4. Pour into pan.
5. Sprinkle dry cake mix evenly over pumpkin mixture.
6. Top with pecans.
7. Drizzle with melted butter (or margarine).
8. Bake at 350°F for 50–55 min or until golden.
9. Let cool completely before serving.
10. Serve with whipped topping.
11. Refrigerate leftovers.

Recipe submitted by Janet Pradarelli and obtained from [Duncan Hines](#).

BIOPHYSICS NEWS

SCIENCE FEATURE

Michael T. Lerch, PhD, assistant professor of biophysics, discusses his research.

Much of my research to date has focused on developing technology that enables site-directed spin labeling (SDSL) electron paramagnetic resonance (EPR) spectroscopy to be performed on proteins at high hydrostatic pressure, which provides unique mechanistic insights by mapping sparsely populated regions of the conformational landscape. Given the location of my lab within the National Biomedical EPR Center, I am well-positioned to continue my technology development work in variable-pressure EPR with the assistance of the excellent engineering staff. My current projects use these and other methods to explore the molecular mechanisms of signal transduction in G-protein-coupled receptors (GPCRs), which are a large and diverse class of cell surface receptors responsible for regulating nearly every physiological process in the human body. GPCRs rely on a high degree of conformational flexibility to achieve their signaling complexity, and one of the major goals in the field of structure-based drug design is to identify the conformations that generate a particular signaling profile. Significant progress toward this goal has been made, yet

relatively little is known about the effects of endogenous modulators including protein-lipid interactions, post-translational modifications, and accessory proteins on GPCR structure and dynamics. Defining the effects of endogenous modulators on the conformational landscape and the interplay of endogenous modulators with potential drugs is a major long-term goal of my lab.

Our current investigations include characterizing the impact of two post-translational modifications, glycosylation and palmitoylation, on β 2-adrenergic receptor (β 2AR) structure and dynamics. The goal for this project is to reveal the molecular mechanisms by which these endogenous modulators regulate β 2AR signaling using a complementary combination of continuous-wave and pulsed EPR techniques, mass spectrometry, and functional assays. In addition to this project, we maintain active collaborations with Profs. Brian K. Kobilka (Stanford) and Robert J. Lefkowitz (Duke) in which we use EPR to explore other important aspects of GPCR signaling, including basal activity, biased signaling, and allosteric ligand-mediated signaling.

Notice: iLab for Use of Liquid Nitrogen

The Department of Biophysics recently began using an Agilent software program called iLab to record and invoice use of liquid nitrogen from the main Biophysics tank. Users will continue to dispense liquid nitrogen into their own containers as usual; however, rather than recording the number of liters dispensed on a paper log, users will now enter the information into iLab via the Chromebook that is in the same room as the tank. Prior to using iLab, each user must be entered into the iLab system. Please contact [Janet Pradarelli](#) with invoicing questions and [Tim Thelaner](#) for technical support.



Dr. Kalyanaraman (left) presenting Dr. Li (right) with the Dean's Award in CITI, which he & Dr. Piero Antuono received for their Alzheimer's disease research.

SEMINAR SERIES

*Our Spring 2019 Graduate Seminar Series takes place **most Fridays** throughout the semester, from **9:30–10:30 am**. Please join us!*

Jan 18 | Michael Dwinell, PhD (MCW), Chemokines in Cancer: Can We Translate into the Clinic?

Jan 25 | Jimmy Feix, PhD (MCW), Membrane Interaction and Activation of the Bacterial Phospholipase, ExoU

Feb 1 | Natalia Stein, PhD (MCW), Biomembrane Fluidity and Heterogeneity by Stretched Exponential

Feb 8 | Tadeusz Sarna, PhD (Jagiellonian University), Sub-lethal Photoc Stress, Modulated by the Age Pigment Lipofuscin, Inhibits Phagocytic Activity of Retinal Epithelium Cell

Feb 15 | R. David Britt, PhD (UC Davis), Spectroscopic Interrogation of Bioassembly Mechanisms of Fe-Fe Hydrogenase and Nitrogenase

Feb 22 | Mahsa Ranji, PhD (UWM), Optical Imaging of Tissue Metabolism and Vasculature

Mar 1 | Quan Jiang, PhD (HFHS), FMRI Detection of Glymphatic Responses after Neurological Diseases

Mar 15 | Murali K. Cherukuri, PhD (NCI), Molecular Imaging of the Tumor Microenvironment

Mar 22 | Sunil K. Saxena, PhD (U-Pitt), Cu(II) as an ESR Spin Label for Protein Structure

Mar 29 | David Hoogerheide, PhD (NIST), Structural Features of Peripheral and Integral Membrane Proteins Revealed by Neutron Reflectometry

Apr 5 | Glenn Millhauser, PhD (UCSC), How Metal Ions in the Brain Tip the Toxic Balance of the Killer Prion Protein

Apr 12 | Arvind P. Pathak, PhD (Johns Hopkins), Towards "Image-Based" Systems Biology - Adventures in Preclinical Imaging, Modeling and Visualization

DEPARTMENT NEWS

Welcome

- Christopher Chitambar (secondary faculty appointment)

Congratulations

- Mona Al-Gizawiy & Kathleen Schmainda: Received a grant from the Children’s Research Institute
- Matthew Budde (Biophysics graduate faculty): Recognized as one of MCW’s outstanding graduate school educators for 2017–2018
- Michael Lerch: Published a paper in [Cell](#)
- Daniel Olson: Received his PhD in Oct. 2018 & accepted a job with GE Healthcare
- Christopher Pawela (Biophysics graduate faculty): Recognized as one of MCW’s outstanding graduate school educators for 2017–2018
- Kathleen Schmainda: Received MCW Cancer Center Director’s Promising R01 Award for her recent R01, “Brain Tumor Treatment Monitoring with the Identification of the Functional Tumor Extent (FTE) using Multi-Parametric MRI”
- Years of service: Cathy Marszalkowski (15 yrs), Guangyu Chen (10 yrs), & Monika Zielonka (10 yrs)

Of Interest

Dara W. Frank, PhD, professor of microbiology & immunology, and Jimmy B. Feix, PhD, professor of biophysics, and their colleagues recently published an exciting article, “[Identification of a ubiquitin-binding interface using Rosetta and DEER](#),” in *Proceedings of the National Academy of Sciences of the United States of America*.

This article is significant because it demonstrates the capability for using double electron-electron resonance (DEER) spectroscopy (Fig. 1) in conjunction with molecular modeling to identify a protein-protein interaction interface. Protein-protein interactions control almost every facet of cellular signaling, involving highly specific complementary binding surfaces. Accurately identifying sites of protein-protein interactions is a challenging problem in structural biology. The current study identified a binding interface between ubiquitin and ExoU, an important virulence factor in certain bacterial infections (Fig. 2). Knowledge of this binding interface may allow the development of drugs to prevent the ExoU-ubiquitin interaction as a novel approach to new antibiotics. Other authors include Maxx H. Tessmer, Adam M. Pickrum, and Molly O. Riegert from the Department of Microbiology & Immunology, and David M. Anderson, PhD, Rocco Moretti, PhD, and Jens Meiler, PhD, from Vanderbilt.

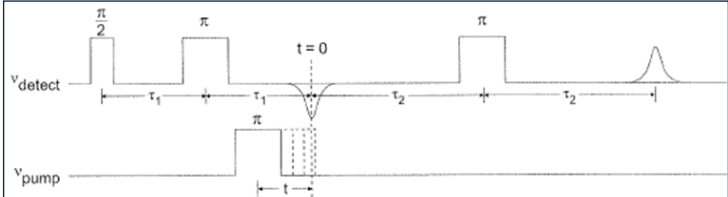


Figure 1. The DEER pulse sequence uses two microwave frequencies. Magnetic dipole-dipole interactions between pumped and detected spins allows determination of spin-spin distance distributions.

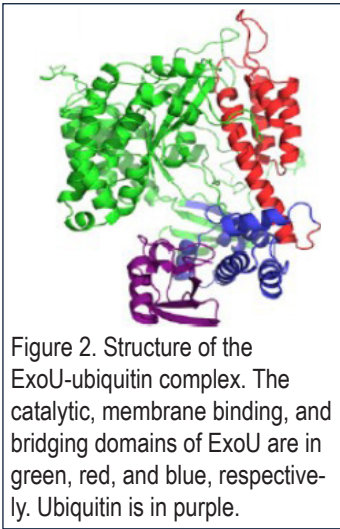


Figure 2. Structure of the ExoU-ubiquitin complex. The catalytic, membrane binding, and bridging domains of ExoU are in green, red, and blue, respectively. Ubiquitin is in purple.

Growing up in Germany, we always had nutty treats for the Advent and Christmas season (hazelnut tortes, cinnamon star cookies, almond nut bars, etc.). After moving to the United States, I always loved the idea of pecan pie, but, just like Goldilocks, I never found a recipe that was quite right—until seeing this one on an episode of *Cook’s Country* on PBS several years ago. I made it that year for a family get-together, and it was immediately devoured. But because one pie only yields so many slices, I have since changed it up and now make the tartlets instead. They store well for up to a week at room temperature in an airtight container, but they never last that long. Enjoy! –Mona

RECIPE

Pecan Tartlets

Submitted by Mona Al-Gizawiy

Yield ~72

Ingredients

- 1 cup Lyle’s golden syrup
- 1 cup light brown sugar, packed
- 1/2 cup heavy cream
- 1 tablespoon molasses (optional)
- 4 tablespoons unsalted butter (cold)
- 1/2 teaspoon salt
- 6 large egg yolks
- ~3 cups pecans, toasted & coarsely chopped
- pie crust/shell (chilled)

Directions

1. Preheat oven to 450°F.
2. Over medium heat, combine syrup, sugar, cream, and molasses (if using), stirring occasionally until sugar dissolves, 3 to 5 min.
3. Remove from heat and set aside for 5 min.
4. Whisk in butter and salt.
5. Whisk in egg yolks until well combined, taking care not to scramble them. (Note: If the eggs curdle a little, keep whisking and then strain it all into a new bowl. It’s very forgiving!)
6. Remove pie dough from fridge, roll it out, and cut out 2.75-inch rounds of dough. (Note: The 2.75-inch rounds fit perfectly into the wells of my jam tart/ mince pie pans. If using standard muffin tins, the rounds may need to be a bit larger.)
7. Place the dough rounds into lightly greased wells of jam tart molds (or similarly sized muffin tin wells).
8. Add 1–2 tsp. of pecans to each tartlet (depending on how finely/coarsely they were chopped) and carefully pour in syrup mixture (about 1 tbsp. each, just enough to cover the pecans). (Note: Take care not to overfill them.)
9. Put the tartlets in the oven on the center rack, and immediately reduce heat to 325°F.
10. Bake for ~25 min. (Note: Baking time varies between ovens. Start checking them at ~20 min. if your oven runs on the hot side.)
11. Remove from oven and cool in pan for 5 min.; then, cool on a wire rack for 1–2 h.
12. Serve with vanilla ice cream or whipped cream (or both!).

Adapted from “old-fashioned pecan pie” recipe by *Cook’s Country*.

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BIOPHYSICS NEWS

SCIENCE FEATURE

Kathleen M. Schmainda, PhD, professor of biophysics, discusses her research.

My research focuses on the development of MRI methods to improve the treatment management of brain tumor patients. The goal is to obtain information about tumor biology (blood vessels and tumor cell proliferation) that is not available with current MRI methods.

Using high-speed MRI technology, we collected data during the administration of a contrast agent. From these data, we developed specialized processing schemes to create blood volume maps of a patient's brain and tumor. We published the first paper showing that this is possible; the paper also provides important information about tumor biology and aggression. This work led to a US Patent and the formation of two MCW start-up companies; also, it is the method of choice for past and ongoing multicenter clinical trials. One of the start-up companies, Imaging Biometrics LLC, has sever-

al FDA-cleared products, one of which is based on this initial work.

Recently, we developed a new imaging biomarker called fractional tumor burden (FTB), derived from our blood volume and tumor burden images. Using our brain tumor bank, we confirmed that FTB can distinguish tumor from treatment-related changes on imaging. We are excited about this development because it addresses one of the most difficult questions facing treating physicians today.

Almost 10 years ago, we used machine learning to develop an extremely promising CAD (computer-aided-detection) method to identify infiltrating brain tumor—a longstanding goal of my research. Now we are leveraging the latest advances in AI (deep learning) to take this work to the next level, with the potential for immense impact on surgical and radiation treatment planning.

NEW CENTER

MCW Center for Disease Prevention Research

MCW recently announced the launch of the new Center for Disease Prevention Research, which will focus on cutting-edge basic, translational, and clinical research for the prevention of major chronic diseases, including cancer, neurological diseases, cardiac diseases, gastrointestinal disorders, and type 2 diabetes.

Headed by Drs. Ming You (director), Balaraman Kalyanaraman (associate director), and Stuart Wong (associate director), the mission of the Center for Disease Prevention Research is to reduce the burden of major chronic diseases by elucidating the mechanisms of preventive modalities, thereby providing a scientific rationale for the design of new and more effective approaches for the prevention of chronic diseases.

By 2030, the aging population (>65 yrs) will increase to more than 70 million, and many will have chronic diseases that adversely affect quality of life. The goal of the MCW Center of Disease Prevention Research is to become a campus-wide catalyst for research focused on the prevention of chronic diseases, and to become a national leader in advancing the science of disease prevention research.

The Center for Disease Prevention Research will collaborate with Froedtert Hospital to establish a new “integrative medicine clinic,” which will provide patients access to conventional and complementary alternative medicine therapies, as well as opportunities to participate in clinical prevention trials.

The Center for Disease Prevention Research is an exciting development for collaborative research at MCW.

VOLUNTEER OPPORTUNITY

Engaging with Your Community

Biophysics is partnering with Cell Biology, Neurobiology and Anatomy (CBNA) to align itself with MCW's mission of community engagement. As part of this effort, Biophysics and CBNA will work with Hunger Task Force to serve local communities.

Many areas within Milwaukee can be described as food deserts, that is, “urban area[s] where it is difficult to buy affordable or good-quality fresh food.” Inhabitants of these areas often face food insecurity, which means they are “without reliable access to affordable, nutritious food” and may know not know when or where they will have their next meal.

MCW is vitally aware that disparities in health can be directly related to disparities in basic needs such as healthy food access and is working with Hunger Task Force's “[mobile market](#)” to help correct this issue. The mobile market is a traveling grocery store that offers foods for purchase—such as fresh produce, meat, and dairy—that are not readily available in food deserts.

Janet Pradarelli (Biophysics) and Virginia Moths (CBNA) are organizing a monthly volunteer opportunity, wherein groups of three volunteers work in 90-min shifts to assist shoppers at the mobile market. The inaugural shift is Tues., June 18, from 10:30 am until noon at the St. Peter's Apartments parking lot on 80th Street in Milwaukee. The first group of volunteers comprises organizers Janet and Virginia and department chairs Balaraman Kalyanaraman (Biophysics) and Jonathan Marchant (CBNA).

Watch for additional information from Janet and Virginia, as they begin assembling volunteers for the monthly commitment. Please consider volunteering for this opportunity to help others in our communities.

DEPARTMENT NEWS

Welcome

- Jacob Benoit (student worker, Li lab)
- Samuel Bobholz (graduate student, LaViolette lab)
- Jonathan Cobb (SPUR student, Schmainda lab)
- Erich Stauder (research technologist I, Zielonka lab)
- Laura McOlash (research technologist III, Dwinell & Kalyanaraman labs)
- Briana Meyer (graduate student, Budde lab)

Congratulations

- Mona Al-Gizawiy won the third place research award at the Sixth Annual Pediatric Cancer Symposium: Tumor Microenvironment for her poster titled “Novel iron-targeted therapy impairs tumor growth and extends disease-specific survival in a xenograft model of recurrent glioblastoma.”
- William Antholine & Jeannette Vasquez Vivar published a [paper](#) in *International Journal of Molecular Science*.
- William Antholine published another [paper](#) in *International Journal of Molecular Science*.
- Gang Cheng, Micael Hardy, Monika Zielonka, Jacek Zielonka, & Balaraman Kalyanaraman published a [paper](#) in *Nature Communications*.
- Jimmy Feix published a [paper](#) in *Biochemistry*.
- Balaraman Kalyanaraman published a [paper](#) in *Carcinogenesis*. He also received the MCW Cancer Center’s Director’s Award for Highly Promising Peer Reviewed Cancer Research for his project titled “Targeting metabolic reprogramming and OXPHOS as a viable anti-melanoma strategy.”
- Shi-Jiang Li, Gang Chen, Guangyu Chen, & Doug Ward published a [paper](#) in *Aging*.
- Kathleen Schmainda & Melissa Prah published a [paper](#) in *Tomography*.
- Karol Subczynski published a [paper](#) in *Nutrients*.

MCW Commencement 2019

Daniel Olson graduated with his PhD in Biophysics.
Nathan Skinner (who received his PhD in Biophysics in 2017) graduated with his MD.

Did You Know?

- The MCW library offers helpful research resources:
- The [funding](#) page allows researchers to search for funding opportunities by text, sponsor, or keyword. Also, researchers can browse an interactive chart using keywords.
 - The [publishing](#) page offers resources to help authors determine the best journal in which to publish.
 - The [poster printing services](#) page offers tips on effective poster design.

The Office of Research and the Clinical & Translational Science Institute offer external review of R01 grant proposals. Details of the program, as well as deadlines for submission for review are available on the [program website](#).

Friendly Faces in Faraway Places

Kathleen Yin, current Center for Imaging Research and former Biophysics employee, and her family recently vacationed in Portugal, where she came across an unexpected, yet familiar face. While browsing at the Lello bookstore in Porto, Kathleen ran into Jason Sidabras, former Biophysics engineer and graduate student, who currently lives in Germany. The reunion was documented (*right*).



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RECIPE

Purslane Salad with Cherries & Feta



4 servings

Ingredients

- 1 generous bunch (about 4 cups) of [purslane](#),* thick stems cut away
- 1 tablespoon fresh mint, chopped
- 22 cherries, pitted and quartered
- 12 kalamata olives, pitted and chopped
- 1 tablespoon sherry vinegar
- 1 tablespoon balsamic vinegar
- 1 tablespoon fresh lemon juice
- 1 small garlic clove, pureed
- ¼ cup extra virgin olive oil
- Salt to taste
- Freshly ground black pepper to taste
- 1–2 ounces feta, crumbled

Preparation

1. Toss together the purslane, two teaspoons of the mint, the cherries, and the olives in a large bowl.
2. Make dressing: Whisk together the vinegars, lemon juice, garlic, olive oil, salt, and pepper.
3. Toss the salad with the dressing. Sprinkle the feta and remaining mint on top.

Obtained from [New York Times Cooking](#).

*Purslane is an annual succulent that is often overlooked as a weed. However, it is dense with nutrients, low in calories, and delicious (tasting vaguely of citrus)! Purslane can be found growing in garden beds, along roadsides, and in other disturbed sites. If foraging for purslane, make sure to gather it from an area free from pesticides.

BIPHYSICS NEWS

SCIENCE FEATURE

Neil Hogg, PhD, Professor of Biophysics; Director, Redox Biology Program; & Associate Dean of Academic Affairs, Graduate School of Biomedical Sciences, discusses his research.

Nitric oxide was first introduced to me as a biological mediator (rather than an atmospheric pollutant) during my PhD studies at the University of Essex and the Wellcome research institute in the United Kingdom. I have remained fascinated by this diatomic free radical, and how its unique biological chemistry allows a multiplicity of biological outcomes. Despite rumors to the contrary, nitric oxide is an extremely stable molecule, and its unique biological role derives from its selective reactivity. As an intrinsically stable free radical (i.e., one that will not rapidly react with itself, and one that will not readily steal electrons/hydrogen atoms from biological molecules), it *selectively* reacts with other free radicals and certain transition metal ions. Its diffusion-limited reaction with the free radical superoxide to form peroxynitrite (a very strong and relatively unselective oxidant) is a key example that we have studied in detail. Its interaction with metal ions—exem-

plified by its canonical mechanism of guanylyl cyclase activation, but also apparent in its reactions with hemoglobin, with metal sites in the mitochondrial electron transport chain, and with other heme iron/non heme iron groups—allows its influence to be felt in many disparate processes. Further widening its scope, researchers have realized that nitric oxide can drive multiple post-translational oxidative modifications of proteins via nitration, nitrosation, tyrosine dimerization, and even perhaps sulfenylation. In the case of S-nitrosation, this is regarded as a major mechanism through which nitric oxide acts, and one that we have investigated at length. We are currently examining the biological chemistry of the interaction between nitric oxide and the smallest thiol, hydrogen sulfide. In addition, we are examining the mechanism of the fascinating discovery that red light can stimulate nitric-oxide-dependent vasodilation.

SEMINAR SERIES

*Our Fall 2019 Graduate Seminar Series takes place **most Fridays** throughout the semester, from **9:30–10:30 am**. Please join us!*

Sept. 6 | Reza Dastvan, PhD (Vanderbilt), Catching a 'notorious' drug pump in action: Energy transduction, alternating access, and mechanism of allosteric modulation of the multidrug transporter P-glycoprotein

Sept. 13 | Nicolai Lehnert, PhD (Univ. Michigan), The special role of the proximal cysteinate ligand in cytochrome P450 and nitric oxide synthase catalysis

Sept. 20 | William Gross, MD, PhD (MCW), Preventing postoperative language deficits using fMRI and ECoG

Sept. 27 | Albert van der Vliet, PhD (Univ. Vermont), The DUOX paradox: Contrasting roles in allergic airways disease and age-related lung pathology

Oct. 4 | Tracy Young-Pearse, PhD (Harvard), Probing heterogeneity in Alzheimer's disease and the aging human brain using iPSCs

Oct. 25 | Jarett Wilcoxon, PhD (UWM), Nitrogenase cofactor biosynthesis: A complex cofactor for a challenging reaction

Nov. 1 | Alexander Helfand, MS (MCW), Quantitative assessment of language lateralization in the brain by fMRI: Methods and findings

Nov. 8 | Shi-Jiang Li, PhD (MCW), Pharmacological prevention of Alzheimer's disease

Nov. 15 | Seung-Yi Lee, MS (MCW), Magnetic resonance imaging biomarkers for cervical spinal cord injury in rats

Nov. 22 | Jai-Qing (Tony) Tong, MS (MCW), Mapping multimodal convergence zones using representational similarity analysis and a high-dimensional grounded model of conceptual content

COMMUNITY ENGAGEMENT

Mobile Market Update

In June, the Biophysics and Cell Biology, Neurobiology & Anatomy departments participated in their inaugural volunteer opportunity with the [Hunger Task Force's Mobile Market](#), which provides fresh and healthy foods to communities that have limited access.

The departments have since decided to "adopt" the site, which is located at St. Peter's Apartments in Milwaukee. This means that each month, three volunteers will visit the site and help the Hunger Task Force distribute groceries from the Mobile Market to shoppers from the community. To date, 11 individuals from the two departments have volunteered, and six volunteers are scheduled to partici-

pate in the next two months. If you are interested in volunteering in the future, contact [Janet Pradarelli](#).



DEPARTMENT NEWS

Welcome

- Alex Garces (graduate student, Lerch lab)
- Matea Juric (research technologist, Zielonka lab)
- Stephen Mazurchuk (graduate student, Binder lab)

Farewell

- William Antholine (professor): Dr. Antholine has retired! However, he will continue to participate in Biophysics as a volunteer faculty.
- Jacob Benoit (student worker, Li lab)
- Jonathan Cobb (SPUR student, Schmainda lab)
- Christian Elliehausen (research technologist, Hogg lab)
- Naiara Herrera (graduate student, Vasquez Vivar lab)
- Bonnie Jin (student worker, Li lab)
- Laxman Mainali (research scientist, Subczynski lab)
- Sarah Oehm (postdoctoral fellow, Kalyanaraman lab)
- Jose Palomares (medical student, Schmainda lab)
- John Schneider (research technologist, Klug lab)
- Eric Stauder (research technologist, Zielonka lab)



Congratulations

- William Antholine: Published a [paper](#) in *International Journal of Molecular Sciences*.
- Guangyu Chen, Doug Ward, Shi-Jiang Li: Published a [paper](#) in *PLoS One*.
- Gang Cheng, Jacek Zielonka, Balaraman Kalyanaraman: Published a [paper](#) in *Oncotarget*.
- Neil Hogg: Published a [paper](#) in *Molecular Cellular Biology*.
- Balaraman Kalyanaraman: Published a [paper](#) in *Breast Cancer Research*.
- Candice Klug: Was awarded an NIH S10 shared instrumentation grant to support state-of-the-art upgrades to the National Biomedical EPR Center's Bruker Q-band E580 pulse EPR spectrometer. Also, was awarded an NIH NIGMS R01 renewal grant.
- Michael Lerch: Was awarded an NIH NIGMS R01 grant.
- Shi-Jiang Li: Was awarded an administrative supplement for his UF1 grant.
- Richard Mett, James Anderson, Candice Klug, and James Hyde: Published a [paper](#) in *Journal of Magnetic Resonance*.
- Kathleen Schmainda: Was awarded an NIH NCI U01 renewal grant. Also, is a semi-finalist in [AuntMinnie.com's 2019 edition of the Minnies](#), and has been nominated in two categories: Most Influential Radiology Researcher & [Science Paper of the Year](#).
- Kathleen Schmainda, Melissa Prah: Published a [paper](#) in *American Journal of Neuroradiology*.
- Natalia Stein: Published a [paper](#) in *Journal of the American Chemical Society*.
- Natalia Stein, Laxman Mainali, James Hyde, and Karol Subczynski: Published a [paper](#) in *Applied Magnetic Resonance*.
- Jeannette Vasquez Vivar: Published a [paper](#) in *Developmental Neuroscience*.

• • • • •
Kathleen Schmainda is a member of the European COST Action in Glioma Imaging investigative team, which has been accepted for funding by the European Union. Dr. Schmainda was asked to join the team because of her expertise in glioma imaging and work with the NCI quantitative imaging network.

Let's Crush Cancer Together: The second annual Cancer Crush is fast approaching! Mark your calendars for the event on September 28, which will be held on the MCW grounds. The Biophysics Department's team name is *Free Radicals*. So far, we have 29 members, 19 of which will either walk or run the 1 mile or 5k, and 10 that have made donations to the cause. MCW encourages each team to reach \$500 in donations, and we have exceeded that goal! So far, we have raised more than \$900. Thanks to all that have been involved! Those still interested can [sign up today!](#)

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RECIPE

Zucchini Quesadillas



Servings: 6 quesadillas | Time: 35 minutes

Ingredients

- 3 tablespoons olive oil, plus more for frying
- 2 or 3 cloves garlic, thinly sliced
- 1/2 teaspoon red pepper flakes
- 1 1/2 pounds zucchini, grated
- kosher salt
- 1 lime, halved
- 6 ounces grated monterey jack cheese
- 12 6-inch corn tortillas
- sliced avocado, chopped fresh cilantro, additional lime, thinly sliced jalapeno

Directions

Heat a large skillet over medium. Once hot, add oil. Once oil is hot, add garlic and cook, stirring until just golden at the edges, about 1 minute. Add zucchini, 1 teaspoon kosher salt, and red pepper flakes and increase heat to medium-high. Cook, stirring occasionally, until zucchini becomes soft and starts to break down, about 5 minutes. Reduce heat slightly and cook 7 to 10 minutes more, until zucchini is jammy and very tender. Taste for and adjust seasoning. Add the juice of half a lime and scrape mixture into a bowl. Let cool slightly.

Add cheese to zucchini mixture and mix. Lay out 6 of your tortillas and divide the filling among them, going all the way to the edges. Place remaining 6 tortillas on top.

Heat a large skillet over medium and add a couple teaspoons of oil. Transfer assembled quesadillas to the skillet and cook until deeply golden and crisp underneath. Flip quesadilla(s) and repeat on second side. Squeeze the juice of the remaining lime half over them.

Serve halved or in wedges with additional avocado, cilantro, lime wedges, and jalapeno.

Recipe obtained from [Smitten Kitchen](#).

BIOPHYSICS NEWS

SCIENCE FEATURE

Jacek Zielonka, PhD, DSc (assistant professor of biophysics), discusses his research interests.

My research focuses on the development of chemical biology tools to modulate and detect cellular reactive oxygen and nitrogen species, including superoxide, hydrogen peroxide, and peroxynitrite (ONOO⁻). Our lab activity ranges from basic chemistry and reaction kinetics to cell-free enzymatic systems to cultured cells *in vitro* and animal models *in vivo*. The overall goal of this research is to understand the role of cellular oxidants in cell function and dysfunction, and to develop redox-based therapeutic strategies.

My current projects focus on the development of novel anticancer agents that target cancer cell bioenergetics and redox status. We have designed and synthesized new compounds capable of inhibiting mitochondrial respiration and, at the same time, catalytically producing reactive oxygen species. These compounds show antiproliferative and cytotoxic activity against various cancer cells *in vitro* and tumor growth inhibitory effects in mouse models of pancreatic cancer *in vivo*.

In parallel, we are working on the development of novel probes for cellular oxidants and are exploring the oxidative chemistry of aromatic boronates

and their use as molecular probes for cellular oxidants and as potential redox-activated prodrugs. Based on the unique chemistry of the interaction of boronate probes with ONOO⁻, we have developed the first ONOO⁻-specific marker product, which can distinguish ONOO⁻- and myeloperoxidase-dependent cellular nitration pathways. This is important for developing therapeutic strategies in cardiovascular diseases and neurodegeneration. Furthermore, we are investigating the oxidative chemistry of boronate-based iron prochelators as potential protective agents in diseases associated with iron-dependent oxidative damage, and we are developing new redox-activated agents, taking advantage of the unique chemical reactivity of boronate compounds.

Also, using the assays developed in our lab to detect superoxide and hydrogen peroxide in a high throughput manner, we are collaborating on the development of new inhibitors of NADPH oxidase-2 for their potential application as protective and therapeutic agents in neurodegenerative and cardiovascular diseases.

WE'RE CRUSHING IT

Thank you to the members of Biophysics' second annual Cancer Crush team, Free Radicals, for their participation and fundraising in the fight against cancer, and to team captain, Janet Pradarelli, for her efforts and encouragement!

Team Free Radicals raised \$1,081, more than doubling its fundraising goal of \$500 and exceeding last year's fundraising efforts by 35%. See page 2

for a graphical representation: Cancer Crush by the numbers.



RECAP: KRAKOW WORKSHOP

MCW researchers participated in the **XIth International Workshop on EPR in Biology and Medicine**, held Oct. 6–10. The conference was jointly organized by Jagiellonian University and MCW, and was co-chaired by Tadeusz Sarna, PhD (professor of biophysics at Jagiellonian University, and visiting professor in the Department of Biophysics, MCW), and Balaraman Kalyanaraman, PhD.

The workshop reviewed progress in EPR instrumentation and methodology, and brought together 125 registrants from 15 countries. The keynote talk was presented by James Hyde, PhD. Biophysics speakers included Natalia Stein, PhD; W. Karol Subczynski, PhD; Jeanette Vasquez Vivar, PhD; and Jacek Zielonka, PhD. Additional speakers from MCW included Zeljko Bosnjak, PhD; Kulwinder Dua, MD; Albert Girotti, PhD; Witold Korytowski, PhD; and Bo Wang, PhD.

Again this year, arrangements have been made with Larry Berliner, editor-in-chief of *Cell Biochemistry and Biophysics*, to publish a special issue devoted to the workshop. *CBB* publishes papers in biochemistry and biophysics, oxidative stress, as well as spectroscopic and innovative instrument design.

Eleven EPR workshops have been organized in Krakow since 1989. The 1st International EPR Workshop was organized by Dr. Subczynski (who was then on the faculty of biophysics at Jagiellonian University) in conjunction with the conferment of the honorary doctorate degree from Jagiellonian University to Prof. James Hyde. This collaborative effort between MCW and Jagiellonian University researchers has resulted in hundreds of scientific publications, and recruitment of graduate students, post-doctoral fellows, and visiting professors to MCW.


DEPARTMENT NEWS

Welcome

- Gage Stuttgart (IDP rotation student [Nov. 4–Dec. 13], Lerch lab)
- Aleksandra Grzelakowska (postdoctoral fellow, Zielonka lab)
- Malory Mueller (research technologist I, Klug lab)
- Zheng Yang (international collaborator, Li lab)

Congratulations

- Samuel Bobholz: Won a Research Day 2019 [Poster Session Honorable Mention](#).
- Guangyu (Gary) Chen: Received the 2018 Investigator of the Year Award from the Alzheimer Association Southeastern Wisconsin Chapter. Also, the Moore Inventor Fellows Nomination Committee selected his application to move forward as one of two submissions representative of MCW.
- Jimmy Feix & Samantha Gies: Published a [paper](#) in the *Journal of Biological Chemistry*.
- Candice Klug & Michael Lerch: Received AHW Limited Needs Funding Award.
- Briana Meyer: Won a Research Day 2019 [Poster Session Award](#).
- Kathleen Schmainda: Received the Dean of the School of Medicine CTSI Award.
- Jacek Zielonka: Received a supplementary award from the American Cancer Society and MCW Cancer Center.
- Jacek Zielonka & Eric Stauder: Published a [paper](#) in *PNAS*.



1,700
total participants

119
teams

20 + 13
Biophysics employees
family/friends formed the team
"Free Radicals"

Biophysics' team ranked in top **1/3** in funds raised

2nd Annual Cancer Crush
fundraiser for lifesaving cancer research at
Froedtert & Medical College of Wisconsin

HELP SCIENCE CRUSH CANCER | **Saturday, 9/28 2019**

1-mile / 5 K run/walk
on MCW-MKE campus

1 in 2.6
people are expected to develop cancer during their lifetime

>1,600
people in Milwaukee County will likely die from cancer this year

\$379,615 total raised in 2019
as of press time

\$1,081 raised by Biophysics in 2019

\$800 raised by Biophysics in 2018

RECIPE

Turmeric Ginger Chicken Soup



Serves: 4

Ingredients

- 3½–4-pound chicken
- 2 medium onions, unpeeled, quartered
- 2 heads of garlic, halved crosswise
- 4-inch piece ginger, unpeeled, thinly sliced
- 3 dried bay leaves
- 2–3-inch piece fresh turmeric, thinly sliced (or substitute 1 tablespoon ground turmeric)
- 2 teaspoons black peppercorns
- 2 teaspoons coriander seeds
- Kosher salt
- 12 ounces carrots (about 4 medium), peeled, cut into ½-inch pieces on a diagonal
- 8 ounces dried udon noodles
- Scallions, very thinly sliced (for serving)
- Chili oil (for serving)

Directions

Place chicken, onions, garlic, ginger, bay leaves, turmeric, peppercorns, coriander seeds, and several pinches of salt in a large pot. Cover with cold water and bring to a boil over medium heat. Reduce heat and gently simmer until an instant-read thermometer inserted into the thickest part of breast registers 155°F, 30–35 minutes. Transfer chicken to a plate and let cool slightly; keep stock simmering. Remove skin from chicken; discard. Pull meat from bones and shred into bite-size pieces; set aside. Return bones and carcass to stock. Increase heat and bring stock to a boil; cook until reduced by about one-third, 15–20 minutes. Season with more salt if needed. Strain stock into a large saucepan; discard solids. Add carrots, bring to a simmer, and cook until tender, about 5 minutes. Meanwhile, cook noodles in a large pot of boiling salted water, stirring occasionally, until al dente; drain and rinse under cold water. Divide noodles among bowls. Add shredded chicken meat to stock and cook just until heated through. Season stock with more salt if needed. Ladle over noodles. Top each bowl of soup with scallions and drizzle with chili oil.

Recipe obtained from [Bon Appetit](#).

Graphic by Jane Thelaner

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BIPHYSICS NEWS

SCIENCE FEATURE

Ubiquitin Binding to the Bacterial Phospholipase ExoU

By Jimmy B. Feix, PhD (*Professor of Biophysics*)

Many pathogens produce and export proteins to facilitate their survival within the host environment. These proteins, termed effectors, are critical in the outcome of an infection. *Pseudomonas aeruginosa*, a Gram-negative bacterial pathogen, which is a leading cause of hospital-acquired pneumonia, produces four important effectors, the most cytotoxic of which is termed exoenzyme U (ExoU). Once activated within the host, ExoU acts as a phospholipase, degrading the component molecules of cell membranes. This enhances the ability of *P. aeruginosa* to spread from the initial site of infection and can inhibit the host immune response. Consequently, ExoU is an important target for the development of antibiotics specific to *P. aeruginosa* and closely-related pathogens. A novel aspect of ExoU's mechanism of action is that it requires interaction with the eukaryotic protein ubiquitin. Recently, in collaboration with the laboratory of Dr. Dara Frank (Microbiology) we used a combination of computational and biophysical methods to identify the ExoU-ubiquitin binding interface (Tessmer et al., *PNAS*, in press). To obtain structural data on the ExoU-ubiquitin complex,

we used site-directed spin labeling EPR, selectively placing one nitroxide probe on ExoU and a second on ubiquitin. We then used DEER (double electron-electron resonance) to measure the distance between the labeled sites. Analysis of a set of nine interrelated distance constraints (led by Maxx Tessmer, a graduate student in the Frank lab) using the Rosetta software platform identified a likely binding interface. Next, mutations were introduced into this interface that were predicted to either inhibit or enhance the ExoU-ubiquitin interaction. The effects of these mutations were verified experimentally both in enzymatic assays and in an infection model using cultured human cells. Future studies will be focused on structural changes in ExoU upon activation, and the identification of compounds to disrupt the ExoU-ubiquitin interaction. Contributors to this work include graduate students Samantha Kohn (Biophysics), Maxx Tessmer, and Adam Pickrum (Microbiology), postdoctoral fellows Tzvia Springer, PhD (Biophysics), and David Anderson, PhD, Molly Riegert (Microbiology); Dr. Frank; and Jens Meiler, PhD (Vanderbilt University). Our research is supported by a grant from the NIGMS.

REGISTER NOW

Second MCW Redox Biology Symposium, April 12–13, 2018

The Second MCW Redox Biology Symposium is rapidly approaching, and seating is limited. [Register now](#) to ensure your attendance!

Confirmed speakers include Marcelo Bonini, Phyllis A. Dennerly, Bruce A. Freeman, Albert Girotti, Yvonne Janssen-Heininger, Kelsey Kalous, Balaraman Kalyanaraman, Christopher Kevil, Nicole Lohr, Julian Lombard, Subramaniam Malarkannan, Lawrence J. Marnett, James Thomas, Rheal A. Towner, Rodney Willoughby, Moua Yang, and Ming You.

More information is available at the [symposium website](#).

Biophysics Holiday Party

Thank you to all who attended the Biophysics holiday party! This fun, annual potluck brings together Biophysics faculty (including secondary, adjunct, emeritus, and graduate faculty), staff, graduate students, postdocs, and good friends to celebrate the holidays and sample a variety of delicious homemade dishes.

SEMINAR SERIES

*Our Spring 2018 Graduate Seminar Series takes place **most Fridays** throughout the semester, from **9:30–10:30 am**. Please join us!*

Jan 12 | Nikolai Mickevicius, PhD (MCW), MRI Methods to Support Precise Radiation Therapy

Jan 19 | Zhongyu Yang, PhD (NDSU), Combining Proteins with Nanomaterials and Polymers: Understanding the Structural Basis of Enzyme Activity Loss Using Electron Paramagnetic Resonance

Jan 26 | Daniel Olson (MCW), Optimization of Advanced Diffusion MRI

Feb 2 | Laxman Mainali, PhD (MCW), Interaction of Alpha-Crystallin with the Fiber-Cell Plasma Membrane in Cataract Formation

Feb 9 | Peter LaViolette, PhD (MCW), Rad-Path Correlation in Brain and Prostate Cancer

Feb 16 | Marcelo Bonini, PhD (MCW), SOD2 Acetylation as a Mitochondrial Pathway to Stemness in Cancer

Feb 23 | Elizabeth Noey, PhD (MCW), Computational Studies of Reaction Mechanisms, Protein Structure & Dynamics, and Drug Design

Mar 2 | Jacek Zielonka, PhD (MCW), Foolproof Detection of Superoxide – Are We There Yet?

Mar 9 | Christopher Pawela, PhD (MCW), Using Neuromodulation to Block Chronic Pain: What Can We Learn from Small Animal Neuroimaging Studies?

Mar 23 | Matthew Budde, PhD (MCW), Translational Spinal Cord MRI: Novel Contrasts and Pulse Sequences

Apr 6 | Alessandro Senes, PhD (UW-Madison), Biophysical and Computational Analysis of Transmembrane Interactions

Apr 20 | Michael Lerch, PhD (MCW), Mapping Sparsely Populated Regions of the β_2 Adrenergic Receptor Conformational Landscape with Pressure-Resolved SD-SL-EPR

Apr 27 | Samantha Kohn & Tzvia Springer, PhD (MCW), Research in Progress: Structure-Function Studies of ExoU Phospholipase

DEPARTMENT NEWS

Welcome

- Marcelo Bonini (secondary faculty appt.)
- Christine Jennings (research tech. II, Lerch lab)
- David Thiebaut (proj. appt., Kalyanaraman lab)

Congratulations

- Jimmy Feix: Published a [paper in PNAS](#)
- Balaraman Kalyanaraman: Published a [paper in The Journal of Organic Chemistry](#)
- Candice Klug: Published a paper in [Nature Communications](#)
- Shi-Jiang Li and B. Douglas Ward: Published a [paper in the Journal of Pediatric Gastroenterology and Nutrition](#)
- Michael Lerch: Published a [paper in PNAS](#)
- Nikolai Mickevicius: Successfully defended his dissertation
- Jason Sidabras (former Biophysics employee): Received the 21st annual JEOL Student Lecture Prize at the 50th annual international Royal Society of Chemistry EPR meeting.
- Zhan Xu: Successfully defended his dissertation

Special Issue of Applied Magnetic Resonance Dedicated to James S. Hyde

The [December 2017](#) issue of *Applied Magnetic Resonance* is a festschrift for James S. Hyde, PhD, professor emeritus of Biophysics, “on the occasion of his 85th birthday.” This special issue includes the “[Autobiography of James S. Hyde](#)” by Dr. Hyde, which contains an overview of his scientific achievements as well as a bibliography of his EPR and MRI publications and patents, separated into sections and topics to provide convenient access to his 432 publications and patents to date. Also included in this special issue are two personal recollections and 15 scientific contributions by researchers who have been influenced by the work of Dr. Hyde. Three of these articles were written by faculty and staff of the Department of Biophysics, including “[EPR Uniform Field Signal Enhancement by Dielectric Tubes in Cavities](#)” by Dr. Hyde and Richard Mett, PhD; “[High-Pressure EPR Spectroscopy Studies of the E. coli Lipopolysaccharide Transport Proteins LptA and LptC](#)” by Kathryn Schultz, PhD, and Candice Klug, PhD; and “[Saturation Recovery EPR Spin-Labeling Method for Quantification of Lipids in Biological Membrane Domains](#)” by Laxman Mainali, PhD, Theodore Camenisch, Dr. Hyde, and Witold K. Subczynski, PhD.

Cores Fair

A representative from the MCW Cancer Center Redox and Bioenergetics Shared Resource will participate in the Cores Fair on Wed., Feb. 28, from 11:30 a.m. to 1:30 p.m. in the Alumni Center, to let MCW researchers know about the services offered including state-of-the-art approaches to monitor cellular oxidizing species and to interrogate cellular bioenergetic function.

International Collaboration

David Thiebaut is a PhD student at the University of Marseille, France, under the guidance of Dr. Micael Hardy, a long-term collaborator of Drs. Balaraman Kalyanaraman and Jacek Zielonka. David is an organic chemist who works to develop new probes to measure superoxide radical anion in cell mitochondria. While at MCW, he is working in the Kalyanaraman lab to determine the identity of the products formed from his probes by different cellular oxidants and characterize the fluorescence properties of the probes and products. He will also test the ability of his probes to detect mitochondrial superoxide in intact cells and optimize their chemical structure for best performance.

Preparing a Successful Grant

The National Institutes of Health has rolled out a new formset (Forms-E) for grants submitted after Jan. 25, 2018. The MCW Office of Grants & Contracts compiled all changes into a [single guidance document](#), which is available on their website.

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RECIPE

Sesame-Glazed Cauliflower Bites

Serves 2–4

Ingredients

Baked Cauliflower

- 1 cup all-purpose flour
- 1/2 teaspoon garlic powder
- 1/4 teaspoon salt
- 1 cup water (plus more as needed)
- 4 cups cauliflower florets

Sauce

- 2 teaspoons vegetable oil
- 1/2 inch ginger, minced
- 2–3 cloves garlic, minced
- 3–1/2 teaspoon honey (to taste)
- 2–1/2 tablespoons soy sauce
- 1 teaspoon rice vinegar
- 2 tablespoons tomato paste
- 1 teaspoon chili paste (e.g., Sriracha)
- 2 teaspoons toasted sesame oil

Garnish

- Toasted sesame seeds
- Chopped green onions

Directions

1. Preheat oven to 425 F, and line two large baking sheets with parchment paper.
 2. In a bowl, stir together the flour, garlic powder, and salt. Stir in 1 c. water (plus more as needed to get pancake batter consistency).
 3. Dip the cauliflower florets into batter, shake off excess, and place florets onto baking sheet. Leave space between florets so that they can get crispy. Bake for 20 min., rotate baking sheets, and then bake for another 5–10 min., until crispy and browned.
 4. Heat 2 t. vegetable oil in a small saucepan. Add garlic and ginger and sauté over medium-low heat for 60–90 sec., or until fragrant. Add remaining sauce ingredients (except sesame oil) and stir well. Cook on medium-low heat for 5 min., or until sauce has thickened slightly. Then, turn heat to low, stirring occasionally to keep from sticking. Stir in sesame oil.
 5. After cauliflower is done baking, gently mix it with the sauce. Spread it back onto the baking sheets, and return it to the oven for 2–4 min. Remove it from the oven, garnish with sesame seeds and green onions, and serve immediately.
- Adapted from a recipe by [Yup... It's Vegan](#).

BIOPHYSICS NEWS

JOB WELL DONE, JULIE!

Julie (Strandt) Peay, MRI program manager in the Center for Imaging Research, will retire at the end of June. To honor her impact on MRI research at MCW, we asked James Hyde to share some of his recollections about working with Julie.

One day long ago, Tom Grist and I were having lunch when an idea fell out of the sky and landed on our table. It was 1984, and the first MCW MRI scanner from GE was scheduled to arrive soon. Tom asked about resonators, and I realized that a simple loop around a joint could be resonated at 63 MHz—1.5T. By December when the scanner arrived, we had built knee coils. Preliminary data for a grant were successfully collected later that month. Initial images made the front page of the *Milwaukee Journal Sentinel*. Better yet, we were funded and off and running. Our MRI coil technologist was

Julie (Strandt) Peay. We exploited her unmercifully.

Between 1986 and 1988, 36 papers were published. The formula was easy: Look each other over for useful body parts, make a coil, and publish; do normal anatomy and publish; and then find some pathology and publish. Julie worked for my coil group 4 hours a week—basically from 8 pm to midnight on Mondays. I sat on a stool and watched. She collected all the images. J. Bruce Kneeland, a radiologist, taught us a little segmental anatomy and kept the IRB happy. Andrzej Jesmanowicz and I argued about everything. These

were golden years. Everything was so new and so easy to publish.

Julie taught me to be nice to people—particularly our volunteer subjects. It was a new style for me.

Julie soon learned that the irregular environment of late night research could lead to all kinds of safety hazards that would be unlikely to occur in a smoothly running clinical environment—like a volunteer wheeled in by a haughty resident in an old-fashioned County Hospital wheel chair made of wood and iron. I caught the impending disaster just in time and let out a scream at the startled guy—I think Julie was already running for the red panic button.

Julie became a leading expert among technologists in the country with her thoughtful posters on MRI safety in a research environment. We were proud, if a little uneasy, to have served as her muse. Julie left MCW for a few years, returning in 2003 when she became the MRI program manager responsible for training all investigators about MRI safety issues. I think she really enjoyed bossing all those PhDs around.

The MRI scanner operator is charged with authority to ban access to the scanner and enforce the protocol as defined by the IRB, which in turn derives its authority from NIH. It is a significant responsibility. Over the years, Julie made important contributions to safety from the perspective of the MRI technologist in a research environment.

Julie was active in the Section for Magnet Resonance Technologists (SMRT) of ISMRM. She edited the SMRT newsletter from 2001–2017, served as SMRT Annual Meeting Program Chair in 1997 and 1998, was elected president of SMRT in 1999, and received the Distinguished Service Award of SMRT in 2006. Her contributions include numerous presentations and posters, often with a focus on safety. —James S. Hyde, PhD (*The James S. Hyde Professor of Biophysics, Emeritus*)

REDOX SYMPOSIUM RECAP

Second MCW Redox Biology Symposium Recap

The Second MCW Redox Biology Symposium took place on April 12–13 at the Medical College of Wisconsin and the Blood Research Institute of the Blood Center of Wisconsin. Total registration for the symposium was capped at 125 participants, and comprised investigators from MCW and the BRI, as well as from neighboring institutions including Aurora Research Institute, Northwestern University, University of Chicago at Illinois, and University of Wisconsin-La Crosse. The opening talk of the symposium was given by Balaraman Kalyanaram and was followed by a poster session and reception. Young Investigator Awards for the two best posters were presented to Kelsey Kalous (graduate student, Department of Biochemistry) and Jennifer Stancill, PhD (post doc, Department of Biochemistry). The symposium presentations covered a wide range of redox biology topics in cancer, cardiovascular, and drug development, highlighting pre-clinical advances and the latest updates in clinical trials.

Feedback received from the attendees' evaluations indicates that the symposium

successfully met its objectives in terms of program content, speakers, sponsors, venues, organization, communication, and opportunities for networking and collaboration.

The symposium was co-chaired by Neil Hogg and Jeannette Vasquez Vivar; Brian Smith and Andreas Beyer comprised the organizing committee; Jane Thelaner coordinated the symposium; Janet Pradarelli, Andrew Barr, and Austin Schoen assisted with preparation of the symposium; and Lydia Washechek maintained the symposium website.

"We are extremely happy with the quality of the science and the interactions between MCW researchers and our invited speakers," said Drs. Hogg and Vasquez Vivar. "We hope to make this a signature event at MCW, so stay tuned for the Third MCW Redox Biology Symposium in a couple of years' time."

The symposium venues were graciously provided by MCW and the BloodCenter of Wisconsin. The symposium was supported by the Advancing a Healthier Wisconsin and the generosity of corporate sponsors.

DEPARTMENT NEWS

Welcome

- Allison Kahlke (research technologist I, Vasquez Vivar lab)
- Jung-Min Park (visiting scientist, Kalyanaraman lab)
- Janet Pradarelli (administrative assistant senior)
- MSTP student: Shana Snarrenberg (Li lab)
- SPUR students: Alexander Zhu (Li lab) & Jessica Jurak (Lerch lab)
- Summer student: Diya Ramanathan (Li lab)

Farewell

- Elizabeth Noey (research scientist I)
- Joseph Ratke (engineer IV)
- Tzvia Springer (postdoc, Feix lab)
- David Thiebaut (proj. appt., Kalyanaraman lab)
- Karthikeyan Thirugnanam (postdoc, Vasquez-Vivar lab)
- Zhan Xu (graduate scientist, Li lab)

Congratulations

- Bill Antholine: Published a paper in [Molecular Cancer Therapeutics](#)
- Gang Chen, B. Douglas Ward, Zhan Xu, Guangyu Chen, & Shi-Jiang Li: Published a paper in [Brain Imaging and Behavior](#)
- Balaraman Kalyanaraman, Gang Cheng, & Jacek Zielonka: Published a paper in [Redox Biology](#)
- Sean McGarry: Received a second year of funding from the CTSI National Research Service Award Training Program
- Richard Scherr: 20 years of service to MCW
- Katie Schultz, Matt Fischer, Elizabeth Noey, Candice Klug: Published a paper in [Protein Science](#)
- Joe Ratke: Retired after 40 years of service
- Jeannette Vasquez Vivar: Published a paper in [Frontiers in Physiology](#)
- Zhan Xu: Published paintings in the [2018 issue of Auscult](#)
- Jacek Zielonka & Balaraman Kalyanaraman: Published papers in [Free Radical Biology and Medicine](#) and [Journal of Leukocyte Biology](#)



Dr. Xu accepts postdoctoral position

Zhan Xu accepted a postdoctoral fellow position at the University of Texas MD Anderson Cancer Center. He will be working in the lab of James A. Bankson, PhD, in the Department of Imaging Physics.

Dr. Balaraman Kalyanaraman receives SAASCR award

Balaraman Kalyanaraman is one of eight Indian American scientists to receive this year’s outstanding achievement award from the Society of Asian American Scientists in Cancer Research (SAASCR). Other award recipients include Subhash C. Chauhan, PhD, Tayyaba Hasan, PhD, Anirban Maitra, MBBS, Priyabrata Mukherjee, PhD, Arun Kumar Rishi, PhD, Selvarangan Ponnazhagan, PhD, and Lalita Shevde-Samant, PhD. The award ceremony took place during the American Association for Cancer Research’s annual meeting in Chicago, IL, on April 15, 2018. SAASCR President Rajvir Dahiya, PhD, presented the honors. The scientists were recognized for their outstanding contributions to cancer research. More than 5,000 scientists from Asia, mainly of Indian origin, working in the United States and Canada in the field of cancer research, are members of the SAASCR.

An [article about the award](#) was published in India West Journal.

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RECIPE

Grilled Asparagus with Miso-Ginger Dressing



Serves 4

Ingredients

- 1 pound asparagus, trimmed
- 2 tablespoons extra-virgin olive oil
- Kosher salt and freshly ground pepper, to taste
- 1 tablespoon white miso
- 1/2 teaspoon grated fresh ginger
- 1 clove garlic, finely minced
- 2-1/2 rice wine vinegar
- 1 teaspoon roasted sesame oil
- 1-1/2 teaspoon honey
- 1 teaspoon sesame seeds

Directions

1. Preheat grill at high heat.
2. Toss asparagus with olive oil, salt, and freshly ground pepper.
3. Place asparagus on grill. Cook, turning occasionally, until well-charred and tender, 5 to 8 min.
4. Transfer asparagus to a serving dish.
5. Whisk miso, grated ginger, minced garlic, rice wine vinegar, sesame oil, and honey in a bowl until smooth. Then, drizzle over asparagus.
6. Sprinkle with sesame seeds.

Loosely based on a recipe from [Savour.](#)

MCW Magazine

The [Winter 2018 issue of MCW Magazine](#) features an article, “Predicting Prostate Cancer: MCW Researchers Seek to Amplify Predictive Powers of Prostate MRI,” about the research of Peter LaViolette, PhD, assistant professor of Radiology, Biophysics graduate faculty, and Biophysics alumni, and Sean McGarry, a biophysics graduate student working in the LaViolette lab.

BIOPHYSICS NEWS

SCIENCE FEATURE

Tadeusz (Tad) Sarna, PhD, DSc, visiting professor of biophysics from Jagiellonian University, Poland, discusses his photobiophysics research.

Even though solar radiation supports life on Earth via photosynthesis and plays a key role in many specific processes, including vision and the entrainment of our biological clock, excessive exposure of the human skin and eye to sunlight could cause adverse reactions leading to distinct pathologies, such as skin cancer, cataract, and age-related macular degeneration.

My Laboratory of Photobiophysics at the Department of Biophysics, Jagiellonian University, in Krakow, Poland, has been involved in studying phototoxic reactions to the skin and eye retina to determine their molecular and cellular mechanisms and to develop efficient protective strategies. Using advanced physicochemical methods—laser flash photolysis, direct singlet oxygen detection, atomic force microscopy and spectroscopy, EPR spin trapping and oximetry—we have demonstrated that the age pigment lipofuscin, which accumulates in the retinal pigment epithelium (RPE), upon irradiation with

blue light generates reactive oxygen species and, therefore, can contribute to oxidative stress conditions in the human retina. Our most recent studies showed that natural antioxidants, such as zeaxanthin and vitamin E, can lower the phototoxic potential of lipofuscin. Employing W-band EPR spectroscopy, available in the National Biomedical EPR Center, we were able to detect distinct paramagnetic changes of human RPE melanin with age, suggesting photooxidative modifications of the melanin pigment. Indeed, such age-related changes have been confirmed by chemical analytical methods. The results are the first unambiguous experimental demonstration that human RPE melanin undergoes substantial structural changes with aging, which lower the photoprotective and antioxidant capabilities of the melanin.

The long-term scientific collaboration between my laboratory in Poland and the Department of Biophysics, MCW, has been both very productive and enjoyable.

SAVE THE DATE

**XIth International Workshop on EPR in Biology and Medicine, Krakow, Poland
October 6–10, 2019**

The XIth International Workshop on EPR in Biology and Medicine will be held in Krakow, Poland, on October 6–10, 2019. The workshop is co-chaired by Balaraman Kalyanaraman, PhD (MCW), and Tadeusz Sarna, PhD, DSc (Jagiellonian University).

Topics to be discussed at the workshop include the following:

- EPR instrumentation and methodology
- Metals in biology
- Site-directed spin labeling/high-pressure EPR
- Synthesis and use of new spin labels and spin traps

- ROS/RNS and oxidative damage
- Free radicals and excited state species in photobiology
- Mitochondrial redox signaling
- Advanced optical imaging and quantitative imaging
- Biophysics of melanin
- Antioxidants and redox signaling
- Atomic force microscopy
- Stem cells and tissue engineering

Visit the website for more information:
www.internationalEPRworkshop.pl.

Email [Jane Thelaner](mailto:jane.thelaner@mcw.edu) to receive important updates.

SEMINAR SERIES

*Our Fall 2018 Graduate Seminar Series takes place **most Fridays** throughout the semester, from **9:30–10:30 am**. Please join us!*

Sept. 7 | Sean McGarry, BS (MCW), Applications of Artificial Intelligence to Brain and Prostate Cancer

Sept. 14 | Guangyu Chen, PhD (MCW), Staging and Predicting Alzheimer's Disease Development

Sept. 21 | Sidhartha Tan, MD (Wayne State), Timing of Perinatal Brain Development and Free Radical Pathogenesis

Sept. 28 | Timothy Meier, PhD (MCW), Neuroimaging and Blood Biomarkers of Sport-Related Concussion

Oct. 5 | Ze Wang, PhD (Temple Univ), Machine Learning for Arterial Spin Labeling Perfusion MRI Signal Processing

Oct. 12 | Christopher Chitambar, MD (MCW), & Kathleen Schmainda, PhD (MCW), Development of an Iron Metabolism-Targeting Drug for the Treatment of Glioblastoma

Oct. 19 | Sruti Shiva, PhD (U Pitt), The Mighty Mitochondrion: A Hub of Redox Signaling

Nov. 2 | Jack H. Freed, PhD (Cornell), Modern ESR at ACERT and Applications in Biophysics

Nov. 9 | Michael Bridges, PhD (UCLA), Exploring the Effects of High Hydrostatic Pressure on Spin Labeled Proteins by Saturation Recovery EPR

Nov. 30 | Yamuna Krishnan, PhD (U Chicago), Quantitative Imaging of Reactive Species

Dec. 7 | Ethan Duwell, BA (MCW), Aberrant Population Receptive Fields in Albinism

Dec. 14 | Brian Bennett, DPhil (Marquette), Biomedical, Translational, and Clinical Applications of Very-Low-Temperature EPR: What, Why, How, and Where Next?

DEPARTMENT NEWS

Welcome

- Sarah Oehm (postdoctoral fellow, Kalyanaraman lab)
- Angela Zhou (summer student, Li lab)

Farewell

- Matthew Fischer (research technologist I, Klug lab)
- Steven Komar (research technologist I, Kalyanaraman lab)
- Kathryn Schultz (research scientist I, Klug lab)

Congratulations

- Gang Cheng, Monika Zielonka, Jacek Zielonka, & Balaraman Kalyanaraman: Published a paper in [Journal of Biological Chemistry](#)
- Jimmy Feix & Samantha Kohn: Published a paper in [Cell Biochemistry and Biophysics](#)
- Neil Hogg: Published a paper in [Free Radical Biology & Medicine](#)
- James Hyde & Richard Mett: Published a paper in [Cell Biochemistry and Biophysics](#)
- Balaraman Kalyanaraman: Published a paper in [Journal of Biological Chemistry](#)
- Michael Lerch: Published a paper in [Immunity](#), received a Research Affairs Committee New Faculty (Pilot) Grant

The Department of Biophysics is pleased to announce the following promotions:

- Jacek Zielonka, PhD, has been promoted to assistant professor. Dr. Zielonka's current research interests focus on the development of new, rapid methods of detection of reactive oxygen and nitrogen species, and application of high-throughput screening for development of new inhibitors of NADPH oxidases and of other enzymes producing reactive oxygen and nitrogen species for cardioprotection, neuroprotection, and cancer treatment.
Dr. Zielonka earned his MSc with honours in chemistry and chemical technology in 1998 and his PhD with honours in chemistry in 2002 at Technical University of Lodz, Poland. In 2015, he earned his DSc in chemical sciences at Lodz University of Technology, Poland. Dr. Zielonka came to the Medical College in 2004 as a postdoctoral fellow in Dr. Balaraman Kalyanaraman's lab. He has continued work in the Kalyanaraman lab, first as a research scientist and then as research director of the Free Radical Research Center. During his career, Dr. Zielonka has co-authored more than 90 peer-reviewed publications. Congratulations, Jacek!
- Monika Zielonka, MSc, has been promoted to the role of lab manager of the Redox & Bioenergetics Shared Resource (RBSR). Ms. Zielonka has long-term experience with cell-based assays and has been working in the Kalyanaraman lab for the past 10 years. Congratulations, Monika!

Jeannette Vasquez Vivar Taught Course at Anna University

In July 2018, Jeannette Vasquez Vivar, PhD, taught a five-day course at Anna University in Chennai, India. The class introduced students to fundamental concepts of redox biology systems, outlined redox metabolism and its bioenergetics and redox cycles, and provided an overview of redox methodologies used in labs as well as redox-based therapies used in clinical trials worldwide.

Get Biophysical! and Help Crush Cancer

Janet Pradarelli is training for the [WhistleStop Marathon](#) in Ashland, WI, in October 2018. She figured she might as well help science crush cancer while she trains, so she started team *Get Biophysical!* in support of the MCW Cancer Crush challenge. If you haven't already done so, please consider joining team *Get Biophysical!*. You can register to walk/run with Janet—she'll be logging her 543rd mile (!!!) on September 22 at MCW Fest—or you can just donate. To do so, visit [mcwcancercrush.com](#), click "Register" or "Donate Now" and make sure to select team *Get Biophysical!*. Total raised (so far): \$653

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RECIPE

Peach Shortbread



Ingredients

- 1 cup white sugar
- 1 teaspoon baking powder
- 3 cups all-purpose flour
- 1/4 teaspoon cinnamon
- 1/8 teaspoon freshly grated nutmeg
- 1/4 teaspoon salt
- 1 cup softened unsalted butter
- 1 large egg
- 2 peaches, pitted and thinly sliced (between 1/8- and 1/4-inch thick)

Directions

Preheat the oven to 375°F.
Butter a 9×13-inch pan, or spray it with a nonstick spray. In a medium bowl, stir together sugar, baking powder, flour, salt, and spices with a whisk. Using a pastry blender, a fork, or your fingertips, blend the softened butter and egg into the flour mixture. It will be crumbly.
Pat 3/4 of the crumbs into the bottom of the prepared pan, pressing firmly.
Tile peach slices over crumb base in a single layer. Scatter remaining crumbs evenly over peaches.
Bake in a preheated oven for 30 minutes, until top is slightly brown and you can see a little color around the edges.
Cool completely in pan before cutting into 24 approximately 2×2 1/2-inch squares. Alternately, the recipe can be halved and baked in a 8×8-inch pan.
Recipe obtained from [Smitten Kitchen](#).

BIOPHYSICS NEWS

SCIENCE FEATURE

William E. Antholine, PhD (associate professor, Biophysics), discusses his research interests.

About one-third of my research involves obtaining better resolution of hyperfine lines in electron paramagnetic resonance (EPR) spectra at low microwave frequencies (Antholine et al. *Int. J. Mol. Sci.* 19:3523-32, 2018). Most of this research has been focused on spectra for cupric ions in prions, particulate methane monooxygenase, nitrous oxide reductase, and cytochrome c oxidase.

Recently, I have focused on obtaining better resolution of cobalt hyperfine lines for high-spin cobalt complexes. (See Figure 1.) I intend to publish several papers and then provide service to others who would like to use the National Biomedical EPR Center to obtain spectra for high-spin cobalt at low microwave frequencies.

The remainder of my research focuses on metal complexes of known antitumor agents and chromium toxicity. Again, EPR is the primary method used in these studies.

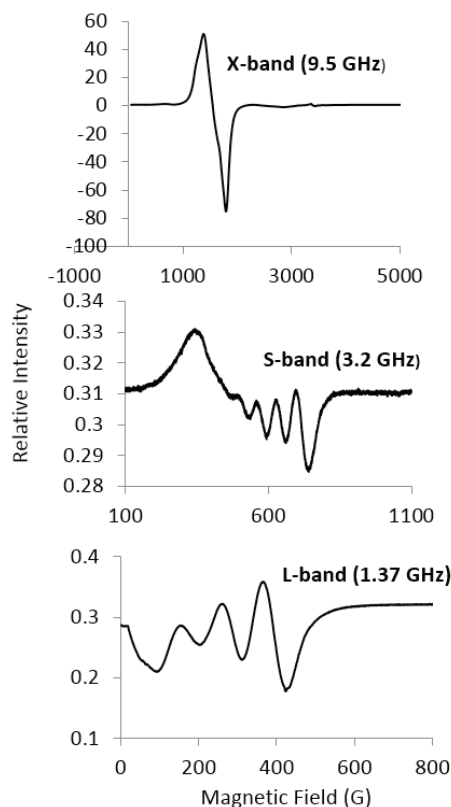


Figure 1. Hyperfine lines in spectra for high spin cobalt resolved using S-band and L-band, but not X-band, microwave frequencies.

An upcoming special issue of *International Journal of Molecular Sciences* titled “EPR Spectroscopy: Applications for Metal Sites in Biological Systems—William E. Antholine at 75” will feature Dr. Antholine and Brian Bennett, PhD, as guest editors. The deadline for manuscript submission is May 31, 2019. Additional details are available on the [IJMS website](#).

DIVERSITY & INCLUSION

MCW’s Office of Diversity and Inclusion offers faculty, staff, fellows, residents, and students the opportunity to attend the National Coalition Building Initiative (NCBI) Welcoming Diversity Exposure Workshop. Through its guided group activities, the workshop encourages attendees to notice the various groups to which we belong, as well as the unconscious biases we have toward different groups, and to consider how these affect our perception and leadership styles. The workshop also encourages attendees to notice

what groups are missing from or underrepresented in different settings. Ultimately, the workshop demonstrates that listening, and being empathetic, to each other is paramount to being able to better understand and respect each other. These ideas are important to consider as we work toward diversity and inclusion.

If you are interested in learning more, you can register for an upcoming NCBI Welcoming Diversity Exposure Workshop [here](#).

CANCER CRUSH

We “Got Biophysical”

Team *Get Biophysical!*, which was spearheaded by Janet Pradarelli, raised a total of \$805 toward MCW’s \$400,000 goal and gathered a group of walkers/runners for MCW’s recent Cancer Crush event. Of the 145 teams that participated, *Get Biophysical!* ranked 48th in funds raised. Thanks, team *Get Biophysical!*, for giving your time and money to fuel cancer research at MCW! Also, special thanks to Janet for organizing and encouraging the team. Not only did Janet’s efforts help raise money for an important cause, the sharing of her personal progress while training for a marathon was both inspirational and motivational toward the personal fitness goals of some team participants.



ATTENTION BIOPHYSICS PERSONNEL

Biophysics Holiday Party

The Biophysics Holiday Party will be held Tues., Dec. 18. Details to follow!

DEPARTMENT NEWS

Welcome

- Kathleen Schmainda (professor) and her lab:
 - Mona Al-Gizawly (research scientist I)
 - Cathy Marszalkowski (clinical research coordinator II)
 - Jose Palomares (medical student)
 - Melissa Prah (engineer II)
 - Robert Wujek (graduate student, BME)
- John Schneider (research technologist I, Klug lab)



Congratulations

- William Antholine: Published a [paper in International Journal of Molecular Sciences](#)
- Gang Cheng, Monika Zielonka, Jacek Zielonka, Balaraman Kalyanaraman: Their recent [article](#) was selected to appear in a special virtual issue of *Journal of Biological Chemistry* that will be assembled in conjunction with the 22nd Symposium on Microsomes & Drug Oxidations.
- Neil Hogg: Published a [paper in Redox Biology](#), and was recognized for 25 years of service to MCW
- Balaraman Kalyanaraman: Posted a [synopsis of a recent review on Science Trends](#)
- Balaraman Kalyanaraman, Gang Cheng, & Jacek Zielonka: Published a [paper in Cell Biochemistry and Biophysics](#)
- Shi-Jiang Li: Received the Dean's Award in Clinical & Translational Research for contributions toward advancing translational science to improve patient health with his Alzheimer's disease research
- Mona Al-Gizawiy & Kathleen Schmainda: Published a [paper in Oncotarget](#), and received a Froedtert Hospital Foundation grant
- Laxman Mainali & Karol Subczynski: Published a [paper in Experimental Eye Research](#)
- Jeannette Vasquez Vivar: Recognized for 20 years of service to MCW, and recognized as one of MCW's outstanding medical student teachers for 2017–2018
- Jacek Zielonka: Published a [foreword in a special issue of Free Radical Biology and Medicine](#), and received an MCW Cancer Center pilot research grant



Drs. Vasquez Vivar & Hogg with their service awards

Groundhog Brownies

Thank you to all who participated in our sixth biannual Groundhog Brownie Day, for which bakers riff on the former Biophysics Administrator Chris Felix's world-famous groundhog brownie recipe. And thanks to Jane Thelaner for organizing it! Bakers: Prepare your ovens (and tweak your recipes) for the next one, which will be held on or around Groundhog Day 2019.



So many delicious brownies!

RECIPE

Pumpkin Chocolate Chip Pancakes



Serves: 2–3

Ingredients

- 1/2 cup + 2 tablespoons all purpose flour
- 3/4 teaspoons baking powder
- 1/4 teaspoon baking soda
- 1/4 teaspoon salt
- 3/4 teaspoon cinnamon
- 1/4 teaspoon ground nutmeg
- 1/4 teaspoon ground cloves
- 1/2 teaspoon ground allspice
- 1/2 cup milk
- 1 egg
- 1 tablespoon butter, melted
- 1/2 cup pumpkin puree (canned or fresh)
- 1/2 cup dark chocolate chips
- warm maple syrup for serving
- butter for serving

Directions

1. In a large bowl, whisk flour, baking powder, baking soda, salt, cinnamon, nutmeg, cloves, and allspice.
2. In a separate, smaller bowl (or a blender), beat milk, egg, melted butter, and pumpkin puree.
3. Pour wet ingredients into dry ingredients and whisk gently to combine. Fold in chocolate chips. Do not overmix.
4. Let the batter rest for 5 min. While the batter rests, heat a large skillet over medium-high heat. Add a little butter to the skillet and then cook pancakes for about 4 min per side until golden brown.
5. Serve with warm maple syrup and butter.

Adapted from a [recipe by PBS food](#).

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BIOPHYSICS NEWS

SCIENCE FEATURE

PRECLINICAL DETECTION OF EARLY ALZHEIMER'S DISEASE RISK ON AN INDIVIDUAL SUBJECT BASIS (Shi-Jiang Li)

Recent clinical trials have demonstrated that, despite extensive evidence to support the amyloid β (A β) cascade hypothesis, drugs targeted at A β have so far failed to reverse deficits in memory or halt cognitive decline. It is possible that cognitive decline may be the result of a complex pathophysiology and that targeting A β alone may not be sufficient and effective in treating Alzheimer's disease (AD). We take a different approach and hypothesize that the neural-network-damaging processes may be an upstream factor during AD progression from the preclinical phase through overt AD dementia. Our neuroimaging data demonstrated that the insidious functional abnormality in the neural network occurred about 20–30 years before the clinical manifestation of AD dementia. This discovery provides a precious window of opportunity for early disease detection and intervention.

Further, we are studying the genetic mechanisms of how the apolipoprotein E (APOE) ϵ gene modulates AD risks. There are three types of APOE variants: ϵ 2, ϵ 3, and ϵ 4 alleles. Individuals with

the ϵ 4 allele are about four times more likely to develop AD than those with the ϵ 3 allele; conversely, the ϵ 2 allele provides a protective effect and individuals with this allele are about four times less likely to develop AD. Although the ϵ 4 allele has been confirmed as a genetic risk factor for AD, not every ϵ 4 carrier will develop AD. The purpose of our study is to identify which, among those cognitively normal ϵ 4 carriers, have a higher risk of developing AD. We found that those ϵ 4 carriers who have higher functional neural activity will have faster episodic memory decline and higher AD risk than those who have lower functional neural activity. Based on these investigations, we should be able to identify those specific ϵ 4 carriers who are at high risk of developing AD and treat them much earlier, before the occurrence of AD dementia. These studies will enhance precision medicine toward secondary AD prevention. For detailed information, please see our recently published articles ([Chen G et al., J Alzheimers Dis. 2016 Oct 4;54\(3\):983-93](#); [Shu H et al., Cereb Cortex. 2016 Apr;26\(4\):1421-9](#)).

TEACHING ABROAD

Balaraman Kalyanaraman traveled to Chennai, Tamil Nadu, India, early in Dec 2016 to teach a course titled "Targeting Cancer Metabolism" at Anna University. This course, which is part of Anna University's recently created Global Initiatives of Academic Network program, comprised a series of six lectures: Overview of cellular metabolism: The Warburg effect and mitochondrial dysfunction; Mitochondria-targeted drugs: Dual targeting of glycolytic and mitochondrial metabolism in cancer; Mitochondrial ROS, redox signaling, and cancer cell proliferation; Factors influencing energy metabolism in cancer: Oncogenes,

hypoxia, tumor suppression, metabolic enzymes, and immune function; Targeting metabolic pathways and metabolic imaging; and Side effects of anticancer drugs: Mitigation by mitochondria-targeted drugs. Originally intended to span six days, these lectures were condensed into two days because the region was shut down first due to the death of the Tamil Nadu chief minister J. Jayalalithaa and then due to Cyclone Vardah.

Dr. Kalyanaraman was hosted by his former postdoctoral fellow Anuradha Dhanasekaran, PhD, associate professor and director and head of the Center for Biotechnology at Anna University.

SEMINAR SERIES

Our Spring 2017 Graduate Seminar Series takes place most Fridays throughout the semester, from 9:30–10:30 am. Please join us!

Jan 13 | Brian Bennett, PhD (Marquette University), Quantitative Information on Mitochondrial Status from EPR of Flash-Frozen Biological Material

Jan 20 | Melissa Skala, PhD (UW-Madison), Optical Imaging of Tissue Structure and Function

Jan 27 | Nathan Skinner (MCW), Novel Diffusion-Encoded MRI for Sensitive Assessment of Spinal Cord Injury

Feb 10 | Balaraman Kalyanaraman, PhD (MCW), Converting One Idea into Multiple, MPI Grants: Helpful Tips and Lessons Learned

Feb 24 | Graham Moran, PhD (UW-Milwaukee), The Biochemistry of Renalase: A Decade of Phantoms

Mar 3 | Guangyu Chen, PhD (MCW), Using Multiple Biomarkers to Disentangle the Progression of Brain Changes in Normal Aging from Those in Alzheimer's Disease

Mar 24 | Kathleen Schmainda, PhD (MCW), Clinical Decision Support for Neuro-Oncology through the Development and Translation of Advanced MRI Technologies

Mar 31 | Sterling Johnson, PhD (UW-Madison), Preclinical Alzheimer's Disease

Apr 7 | Kate Carroll, PhD (The Scripps University), Cysteine-Mediated Redox Signaling: Chemical Tools for Biology Discovery

Apr 21 | Samantha Kohn (MCW), Site-Directed Spin Labeling Studies of the Bacterial Phospholipase ExoU

Apr 28 | Brian Smith, PhD (MCW), Erasing and Reading Epigenetic Lysine Acylation with Sirtuins and Bromodomains

DEPARTMENT NEWS

Welcome

- Brittney Helbig (research technologist, Hogg lab)
- Tzvia Springer (postdoc, Feix lab)

Congratulations

- Feix lab: Published a paper in [The Journal of Biological Chemistry](#)
- Hogg lab: Published a paper in [Nitric Oxide](#)
- Hyde lab: Published a paper in [Review of Scientific Instruments](#)
- Li lab: Published a paper in [Journal of Alzheimer's Disease](#)
- Nathan Skinner: Received an NIH predoctoral fellowship, titled "Novel Diffusion MRI Encoding in Rat Spinal Cord Injury Assessment"
- Subczynski lab: Published papers in [Current Eye Research](#) and [Free Radical Biology and Medicine](#)
- Vasquez Vivar lab: Published a paper in [Nitric Oxide](#)

Years of Service

On Feb 3, three Biophysics employees were honored for their years of service to MCW. Thank you for your commitment and hard work!

- James Anderson, engineer III (15 yrs)
- Rupeng Li, research scientist I (10 yrs)
- B. (Doug) Ward, biostatistician II (20 yrs)

RBSR at Cores Fair

Members of the Redox & Bioenergetics Shared Resource (right) participated in the Office of Research Cores Fair on Feb 9. The RBSR provides state-of-the-art equipment and services to support studies on bioenergetics, metabolism, and redox signaling in cancer and normal cells.



Jacek Zielonka, PhD (co-director), and Steve Komars (lab manager) of RBSR

Biophysical Society

On Feb 11–15, members of Biophysics faculty and staff attended the 61st Annual Biophysical Society Meeting in New Orleans, LA. Candice Klug (of the Klug lab), and Laxman Mainali and Marija Raguz (of the Subczynski lab) presented posters at the meeting.

SAVE THE DATE: CROATIA SYMPOSIUM

The *Second Adriatic Symposium on Biophysical Approaches in Biomedical Studies* will be held Sept 24–28, 2017, in Split, Croatia. This symposium is jointly organized by Marija Raguz (University of Split School of Medicine, Croatia), Balaraman Kalyanaraman (MCW), and Tadeusz Sarna (Jagiellonian University, Krakow, Poland).

The focus and goals of the symposium follow:

- Advanced MR techniques: biological and biomedical applications

- Reactive oxygen and nitrogen species, redox signaling, and bioenergetics in cancer, cardiovascular, and other diseases
- Advanced imaging modalities and bio-marker and biosensor developments
- Drug transport and trafficking in membranes and cells

Additional information will follow!



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RECIPE

Honey-Grilled Chicken with Citrus Salad



Serves 4–6

Ingredients

- 1 c fresh orange juice
- 1/2 c honey
- 3 tbsp rosemary, minced
- Kosher salt and freshly ground black pepper, to taste
- 2 lb skin on chicken, legs and thighs
- 1 1/2 c cilantro leaves and tender stems
- 3 tbsp pistachios, roughly chopped
- 15 pitted dates, halved lengthwise
- 1 blood orange, peeled and sliced 1/4" thick crosswise
- 1 navel orange, peeled and sliced 1/4" thick crosswise
- 1 cara cara orange, peeled and sliced 1/4" thick crosswise
- 1 red grapefruit, peeled and sliced 1/4" thick crosswise
- 1 lime, peeled and sliced 1/4" thick crosswise

Instructions

Mix orange juice, honey, rosemary, salt, and pepper in a bowl; add chicken and toss to combine. Marinate 30 min, or until ready to use. Heat a gas grill to medium. (Alternatively, heat a cast-iron grill pan over medium-high heat.) Remove chicken from marinade, and transfer to grill; cook skin-side down, flipping once, and basting occasionally with remaining sauce, until charred and cooked through, 12–15 min. Transfer chicken to a cutting board, and let rest for 15 min before serving. Meanwhile, toss cilantro, pistachios, dates, and citrus pieces; serve with chicken. (Recipe obtained from [Saveur.com](#).)

BIOPHYSICS NEWS

SCIENCE FEATURE

Jeannette Vasquez Vivar, PhD, professor of biophysics, discusses her research interests.

My research interests concentrate on the redox-based biochemical pathways regulating tetrahydrobiopterin functions and oxidant injury. Tetrahydrobiopterin is ubiquitously produced, but its abundance and metabolism differ greatly in human organ systems. Tetrahydrobiopterin is essential for nitric oxide production, inhibition of superoxide anion radical production from neuronal and endothelial nitric oxide synthase, phenylalanine metabolism, and production of neurotransmitters. Defects in the synthetic enzymes are one known cause of neurological and metabolic dysfunction.

Our lab has studied the developmental biochemistry of the tetrahydrobiopterin pathway in the brain and established that this pathway is a target of antenatal hypoxia-ischemia injury. Using a preclinical translational animal model, we have shown that low developmental tetrahydrobiopterin levels greatly influence brain injury outcomes. Currently, we are testing whether prenatal

interventions prove useful to ameliorate hypoxia-ischemia brain injury. These approaches include the use of neuroprotective strategies.

Earlier studies in our lab investigated the role of tetrahydrobiopterin in increasing nitric oxide in a transgenic murine model we generated, which consists of cardiomyocyte-specific GTPCH overexpression. Allogenic cardiac transplantation enhances nitric oxide production; the specific contribution of cardiomyocytes has been controversial. However, using this GTPCH model, we established that tetrahydrobiopterin decreased inflammatory responses through nitric-oxide-independent mechanisms.

Although tetrahydrobiopterin therapeutics has been considered to ameliorate redox imbalances, cellular uptake and recycling have proven to be a significant barrier. We are studying alternative nongenetic ways to stimulate tetrahydrobiopterin synthesis as a possible therapy solution.

40TH EPR CENTER SAB MEETING

The National Biomedical EPR Center hosted its 40th and final annual scientific advisory board (SAB) meeting on May 4–5. Current board members include SAB Chair Wayne Hubbell, PhD (UCLA); Albert Beth, PhD (Vanderbilt); Gareth Eaton, PhD (Denver Univ); Brian Hoffman, PhD (Northwestern); James Hyde, PhD; Candice Klug, PhD; Ronald Mason, PhD (NIEHS/NIH); David Singel, PhD (Montana State); and Harold Swartz, MD, MSHPH, PhD (Dartmouth).

In 1976, Drs. Swartz and Hyde were awarded funding for the EPR Center under the NIH's P41 mechanism. Dr. Hyde was director through 2016, when

he retired and passed directorship to Dr. Klug. This long-running grant is being sunsetted by the NIH after more than 40 years. As the EPR Center transitions into the future, the goal is to maintain NIH funding through alternative mechanisms for the innovative developments that enable clinical and biomedical applications of EPR spectroscopy to flourish.



Pictured left to right: Dr. Swartz, Dr. Singel, Dr. Hyde, Dr. Klug, Dr. Eaton, Dr. Hoffman, & Dr. Hubbell.

HISTORY

The Biophysics Graduate Program celebrated its 100th graduate—Nathan Skinner, PhD (faculty advisor Matthew Budde, PhD)—on March 28, 2017.

Thirty-five years ago, in 1982, Carol Popp Weingarten, MD, PhD (faculty advisor James Hyde, PhD), was the first student to graduate from what is now the Biophysics Graduate Program.

Biophysics began as the Radiation Biophysics Section within the Department of Radiology, and Dr. Hyde was chief of that section. In 1992, as part of an administrative reorganization, the Radiation Biophysics Section became the Biophysics Research Institute, under the direction of Dr. Hyde. The Institute of Biophysics received department status in 2003, after the board of trustees voted to bring it in line with the other basic science departments.

In January 1995, the MCW Graduate School of Biomedical Sciences was formally established, as was the official Biophysics Graduate Program.

Through its evolution, the Department of Biophysics has remained committed to quality in research and graduate and postdoctoral training.

The Biophysics Graduate Program is designed to assist young scientists in developing the research skills needed to thrive in academic and clinical settings. Biophysics is proud of its long history of successful alumni, who have gone on to become professors, researchers, scientists, engineers, and clinicians, and are leaders in their fields.

DEPARTMENT NEWS

Congratulations

- Balaraman Kalyanaraman, PhD, and Ming You, PhD (MCW Cancer Center): Received a \$3.16 million, multi-investigator R01 grant from the NCI to study the potential for use of Mito-honokiol for the prevention of lung cancer and its metastasis.
- Kalyanaraman lab: Published papers in [Antioxidants and Redox Signaling](#) and [InterFace Focus](#), an invited commentary in [Redox Biology](#), and a review in [Redox Biology](#)
- Klug lab: Published a paper in [Protein Science](#)
- Rupeng Li, MD, PhD: Will begin his residency in Massachusetts General Hospital's Anesthesia Department
- Wenjun Li, PhD: Accepted to University of Wisconsin–Madison medical school
- Nathan Skinner, PhD: Successfully defended his dissertation
- Karol Subczynski, PhD, and collaborator Marta Pasenkiewicz-Gierula, PhD, are recipients of a Harmonia grant by the National Science Center of Poland. The major goal of their research is to obtain detailed information about early steps of Chol aggregation in water and the effect of Chol oxidation products and ions on the aggregates formation and stability where the source of Chol and oxChol molecules is a Chol oversaturated bilayer.
- Subczynski lab: Published a paper in [Foods](#)

• • • • •

Two biophysics graduate students received awards at the Graduate Student Association's first Graduate Student Symposium, held on May 16. Congratulations to Sean McGarry (presentation winner) and Daniel Olson (poster winner)!

• • • • •

As part of Women's History Month in March, Jeannette Vasquez Vivar was interviewed about being a female faculty member and her legacy. In Dr. Vasequz Vivar's interview, [available on the MCW YouTube channel](#), she discusses the open and supportive nature of MCW and her peers; the importance of self promotion; and her desire to share knowledge with, and be a mentor to, young scientists.

CROATIA SYMPOSIUM: UPDATE

The [Second Adriatic Symposium on Biophysical Approaches in Biomedical Studies](#), which will be held September 24–28, 2017, in Split, Croatia, provides an excellent opportunity for learning and collaboration.

The scientific program includes a mix of topics, combining some of the most prominent contributors from the joint fields with complementary but overlapping strengths. The program is designed to encourage interaction and discussion.

Abstracts are being for lecture (invited speakers), short oral, or poster presen-

tations in each of the eight program sessions.

Visit the Symposium's website for additional details on abstracts, accommodations, conference registration, and speakers.



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RECIPE

Roasted Rhubarb & Chia Parfait



Serves 6–8

Ingredients

For chia pudding

- 2 x 13.5 oz cans coconut milk
- 1/4 cup coconut water
- 1/4 cup maple syrup
- 1/3 cup chia seeds

For rhubarb

- 1 bunch rhubarb, leaves trimmed
- 1/4 cup sugar
- 1/4 cup maple syrup
- 1 teaspoon vanilla
- 2 star anise pods

Instructions

- Place 13.5 oz coconut milk, coconut water, chia seeds, and maple syrup in a large bowl. Mix well with a whisk. Cover and refrigerate for three hours.
- Preheat oven to 350°. Line a rimmed baking tray with parchment paper.
- Wash and dry rhubarb stalks. Cut into 2" pieces. Place in a bowl with sugar, maple syrup, and anise. Mix well. Pour onto prepared tray and spread evenly. Roast for 20 min, or until tender and syrupy. Stir in vanilla. Allow to cool completely.
- When ready to assemble, stir 13.5 oz coconut milk through chia pudding. Layer chia pudding and roasted rhubarb into six small glasses. Drizzle some of the syrup over assembled parfaits. Refrigerate until ready to serve.

(Recipe obtained from [cookrepublic.com](#))

BIPHYSICS NEWS

SCIENCE FEATURE

CHOLESTEROL'S ROLE IN EYE LENS HEALTH (Witold Karol Subczynski, PhD)

The extremely high cholesterol (Chol) content of the eye lens's fiber-cell plasma membrane is a unique biochemical characteristic. This Chol content increases with age and is always high enough to saturate the phospholipid bilayer and induce formation of pure cholesterol bilayer domains (CBDs). The need for this is unclear; however, it is evident that the disturbance of Chol homeostasis may induce cataracts. To study the effects of Chol on lens membranes, we used the EPR spin-labeling methods developed at the National Biomedical EPR Center, which provide information about the lateral organization of membranes, allowing us to discriminate coexisting domains and obtain several important membrane properties as a function of the membrane depth. Our studies have allowed us to make a few significant conclusions about the function of Chol in fiber-cell plasma membranes: (1) The extremely high (saturating) content of Chol keeps the bulk physical properties of the fiber-cell membrane consistent and independent

of age-related changes in the phospholipid composition. (2) The CBD provides buffering capacity for Chol concentration in the surrounding phospholipid bilayer, keeping it at a constant saturating level. (3) Any increase in oxygen concentration within the lens interior is a major factor in inducing cataract development. A major finding of our research is that human fiber-cell plasma membranes, because of the high Chol content and the presence of CBDs, form significant barriers for oxygen permeation, helping to maintain lens transparency and protect against cataract formation. We conclude that the high Chol content, formation of CBDs, and formation of Chol crystals should not be regarded as major predispositions for the development of age-related cataracts. This study is funded by a grant from the NEI. The work was accomplished with the help of Justyna Widomska, PhD; Marija Raguz, PhD; Laxman Mainali, PhD; Marta Pasenkiewicz-Gierula, PhD; William O'Brien, PhD; Theodore Camenisch, and James Hyde, PhD.

2017 ALZHEIMER AWARD

Shi-Jiang Li, PhD, received the [2017 Alzheimer Award](#) from the *Journal of Alzheimer's Disease* for his article, "[Staging Alzheimer's Disease Risk by Sequencing Brain Function and Structure, Cerebrospinal Fluid, and Cognition Biomarkers](#)." The award includes a 3" bronze Alzheimer Medal and a cash prize of \$7,500. The findings presented in this article support the network dysfunction hypothesis of Alzheimer's disease (AD). The Li lab created the CARE (characterizing Alzheimer's disease risk events) index to characterize risks associated with AD stages and quantify disease severity on an individual subject basis. The CARE index will provide a critical window of opportunity to intervene with disease-modifying therapy, and it will facilitate clinical

trials by selecting the right segmentation of patient populations based on their disease stages to enrich the response rate and statistical power.

It can also be used to monitor and evaluate treatment efficacy through changes in stage status in individual subjects.

Co-authors of the article include Guangyu Chen, PhD; Hao Shu, MD, PhD; Gang Chen, PhD; B. Douglas Ward, MS; Piero G. Antuono, MD; and Zhijun Zhang, PhD.



SEMINAR SERIES

Our **Fall 2017 Graduate Seminar Series** takes place **most Fridays** throughout the semester, from **9:30–10:30 am**. Join us!

Sept 1 | Zhan Xu (MCW) Spatial Compensated Intra-shot Turbo key-Hole (SCITH) Method Increases fMRI Contrast-to-Noise Ratio and Functional Connectivity Reliability

Sept 8 | Xiaoping Hu, PhD (UC Riverside), Multimodal MR Imaging of Parkinson's Disease: Potential for Early Biomarkers

Sept 15 | Megan Frost, PhD (Michigan Tech), Development of Controlled Nitric Oxide Delivery Materials and Real-Time Direct Measurement of Nitric Oxide from In Vitro Cell Culture

Oct 6 | Neil Hogg, PhD (MCW), Nitrosopersulfide: Gasotransmitters in Union

Oct 13 | Arnold Bakker, PhD (Johns Hopkins), Translational Neuroscience of Episodic Memory Function in Aging and Disease

Oct 20 | Ravinder Singh, PhD (Mayo Clinic), Monitoring of Cortisol—A Natural Steroid Doctors Love and Hate

Oct 27 | Ian Rowland, PhD (UW-Madison), Preclinical MRI at 4.7T

Nov 3 | Jeannette Vasquez Vivar, PhD (MCW), Dynamic Fluctuation of Cellular NADPH as a Regulator of NOX2 Activity

Nov 10 | Candice Klug, PhD (MCW), Insights into the Mechanism of LPS Transport in *E. Coli*

Nov 17 | Karol Subczynski, PhD, DSc, (MCW), Saturation-Recovery EPR: Recent Achievements in Eye Lens Membrane Studies

Dec 1 | Edgar DeYoe, PhD (MCW), Albinism: A Curious Model of Aberrant Brain Connectivity and its Consequences

Dec 8 | William Antholine, PhD (MCW), EPR of Metal Complexes of Known Antitumor Agents: Spectra from 1976 to 2016

Dec 15 | Karthikeyan Thirugnanam, PhD (MCW), Dependency of NOX2 Activity on Cellular Energy Metabolism

DEPARTMENT NEWS

Welcome Graduate Students

- Zachary Boyd (Paulson lab)
 - Alexander Helfand (Binder lab)
- Seung Yi Lee (Budde lab)
 - Jiaqing (Tony) Tong (Binder lab)

New Faculty Hired

Biophysics is excited to announce that Michael Lerch, PhD, will join the department in September as an assistant professor.

Summer Students/Volunteer

Biophysics was pleased to host these summer students/volunteer:

- Bennett/Kalyanaraman labs (Tony Francisco)
 - Hogg lab (Felicia Olawuni)
 - Kalyanaraman lab (Jayla Watkins)
- Klug lab (Kyler Crawford)
 - Li lab (Elizabeth Wong, Zhaoyuan Wu)
 - Vasquez Vivar lab (Aleksandra Zielonka)

Congratulations

- William Antholine, PhD: 40 years of service to MCW
- Jimmy Feix, PhD: Published an article in [ACS Omega](#)
- Balaraman Kalyanaraman, PhD: Selected as inaugural member of MCW Society for Research Excellence
- Shi-Jiang Li, PhD:
 - Received an R21 grant to study the network-level mechanisms for preclinical Alzheimer's disease development
 - Published a paper in [Brain Connectivity](#) (co-authors: Gang Chen, PhD, and B. Douglas Ward, MS)
- Karol Subczynski, PhD, & Laxman Mainali, PhD: Published a [chapter](#) as part of the *Advances in Experimental Medicine and Biology* book series
- Jeannette Vasquez Vivar, PhD:
 - Published papers in [Blood Journal](#), [Redox Biology](#) (co-author: Karthikeyan Thirugnanam, PhD), & [Scientific Reports](#)
 - Participated as guest editor of the special series *Nitric Oxide Synthases—from Genes to Function* in [Nitric Oxide](#)

Two Female Biophysics Professors Honored

Candice Klug, PhD, and Jeannette Vasquez Vivar, PhD, were honored at the Senior Female Faculty Pinning Ceremony in June, as two of the 167 women at MCW who have achieved the rank of professor. Drs. Klug and Vasquez Vivar were the 117th and 141st women, respectively, to become full professor at MCW. Interviews with both professors are featured in an [MCW video](#) highlighting female leadership at MCW.

Guest Teaching at the University of Wyoming

On June 5–9, 2017, William Antholine, PhD, gave lectures on EPR to an audience of 45 faculty and students in the Department of Chemistry at the University of Wyoming.

Kalyanaraman Lab Published a Review Article in *Chemical Reviews*

The Kalyanaraman lab published a [review paper](#) in *Chemical Reviews*, a highly regarded and ranked journal with an impact factor of 47.9. The review is the result of more than a decade of development of novel probes, diagnostic agents, and potential drugs for neurodegenerative diseases and cancer treatment conducted by Biophysics in collaboration with researchers from other MCW departments and other institutions in the United States and abroad.

Targeting mitochondrial function was shown to be an effective strategy for the prevention and treatment of various types of cancer, including breast, lung, and pancreatic, in preclinical rodent models.

The corresponding authors of the review are Balaraman Kalyanaraman, PhD, and Jacek Zielonka, PhD, DSc. Co-authors include Joy Joseph, PhD; Adam Sikora, PhD; Micael Hardy, PhD; Olivier Ouari, PhD; Jeannette Vasquez Vivar, PhD; Gang Cheng, PhD; and Marcos Lopez, PhD.

RECIPE

South Indian Vegetable Korma

Serves 8–10

Ingredients



Veggies

- 1 medium head cauliflower, cut into florets
- 3 zucchini, cubed
- 1 tomato, chopped
- 2 red bell peppers, chopped into large pieces
- 1 large carrot, chopped
- 1 large (or 2 medium) onion(s), chopped
- 6–8 cloves garlic, cut into long pieces
- 2 green chilies, cut into long pieces (seeds removed)
- 1 tbsp ginger paste or grated fresh ginger
- 1/2 cup golden raisins
- 1/2 cup raw cashews
- 2 cans coconut milk
- cilantro leaves

Spices

- 1/2 tsp red chili powder
- 1/2 tsp cumin seeds
- 1 1/2 tsp turmeric powder
- 1 1/2 tsp cardamom powder
- 1 pinch ground cinnamon
- 1 pinch ground cloves
- 2 tsp salt
- 1/2 tsp black pepper
- 3 tbsp vegetable or canola oil

Instructions

1. Steam cauliflower until tender; set aside.
2. Sauté or steam zucchini (until al dente) and tomato; set aside.
3. Heat oil in skillet at medium low to medium heat; sauté garlic, ginger, green chilies, chili powder, & cumin seeds until garlic is soft. (Be careful not to burn.)
4. Add carrots, onion, & red bell peppers, and sauté until al dente.
5. In a small bowl, mix turmeric & cardamom with 1/2 cup of water; add to skillet and continue to sauté veggies.
6. Sprinkle into skillet cinnamon, cloves, salt, & pepper; stir. Then stir in raisins and cashews.
7. In a large pot, combine sautéed veggie/spice mixture from skillet, and cooked cauliflower, zucchini, & tomato. Stir in coconut milk, and simmer on low heat for ~15 min.
8. Garnish with cilantro leaves and serve with chapathi or basmati rice. Bon appétit!

Recipe submitted by Lilian Kalyanaraman

Biophysics News is a quarterly MCW departmental newsletter aimed at enhancing departmental engagement through information and good news sharing. Do you have information you'd like to share—news, a photo, a recipe? [Send it to Lydia.](#)

BIOPHYSICS NEWS

SCIENCE FEATURE

Candice S. Klug, PhD (professor, Biophysics; director, National EPR Center; program director, Biophysics Graduate Program), discusses her research interests.

I use the site-directed spin labeling (SDSL) electron paramagnetic resonance (EPR) spectroscopy technique to study the functional dynamics of soluble and membrane proteins essential to bacterial viability. My expertise in these fields was developed during my graduate training here in Dr. Jimmy Feix's lab at the National Biomedical EPR Center, my postdoctoral work in the laboratory of Dr. Wayne Hubbell at UCLA, and my work for the past 16 years as an independent faculty member here in the Department of Biophysics.

My primary research interests continue to focus on protein structure and dynamics. The major goal of my R01-funded project is to gain insights into the mechanism of lipopolysaccharide (LPS) transport across the periplasm of Gram-negative bacteria to enable rational antibiotic drug design that takes advantage of unique protein folds to an essential bac-

terial process. This research has enabled the structural and functional characterization of the essential bacterial protein LptA and its binding partners LptC and LptDE, along with its ligand, LPS, using SDSL EPR spectroscopy and other complementary biophysical techniques. I also have many ongoing research projects with new and long-standing collaborators on the application of EPR spectroscopy to mammalian proteins such as a ligand-gated ion channel, a visual arrestin, both nonvisual arrestins, and the bacterial glycosyl transferase ArnT. Further, as director of the National Biomedical EPR Center, I am leading the reinvention of the EPR Center toward an applications-focused future to enhance the fantastic resources developed here over the past 40+ years to continue to facilitate the advancement of biomedical knowledge by the scientific community at MCW and nationally.

CROATIA SYMPOSIUM

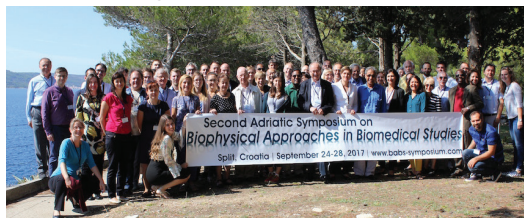
On Sept. 21–28, MCW researchers participated in the Second Adriatic Symposium on Biophysical Approaches in Biomedical Studies in Split, Croatia. The symposium was jointly organized by Balaraman Kalyanaraman, PhD; Marija Raguz, PhD (University of Split School of Medicine); and Tadeusz Sarna, PhD (Jagiellonian University). Jane Thelaner helped coordinate the meeting, and Lydia Washechek compiled the [abstract book](#).

The research presented at the symposium focused on the structure, dynamics, and function of membrane systems and proteins; the role of oxidative stress in human diseases; the detection and imaging of free radicals; and drug transport across membranes. Speakers from MCW included Ivor Benjamin, MD, FAHA, FACC; Zeljko Bosnjak, PhD;

James Hyde, PhD; Dr. Kalyanaraman; Karol Subczynski, PhD; Jeannette Vasquez Vivar, PhD; and Jacek Zielonka, PhD.

An upcoming special issue of *Cell Biochemistry and Biophysics* will be devoted to the symposium, and Dr. Raguz will serve as the guest editor.

This was the second symposium in a series organized in Croatia since 2014. This collaborative effort has resulted in scientific publications and the recruitment of graduate students, postdocs, and visiting professors to MCW.



SAVE THE DATE

Second MCW Redox Biology Symposium, April 12–13, 2018

The Second MCW Redox Biology Symposium will focus on new frontiers in redox biology.

The symposium will kick off the afternoon of Thurs., April 12, 2018, with an opening talk by Balaraman Kalyanaraman, PhD, followed by a poster session for young scientists and trainees. The poster session will provide an excellent opportunity for young participants to share their work and meet our speakers. Refreshments will be served.

On Fri., April 13, 2018, presentations by pioneering researchers and clinicians will highlight advances in areas such as cancer and cardiovascular, inflammatory, and age-related diseases. Breakfast and lunch will be served. Confirmed speakers include Phyllis A. Dennerly, MD; Toren Finkel, MD, PhD; Bruce A. Freeman, PhD; Christopher Kevil, PhD; Lawrence J. Marnett, PhD; Rheal A. Towner, PhD; Eric Verdin, MD; and Ming You, MD, PhD.

The symposium is co-chaired by Neil Hogg, PhD, and Jeannette Vasquez Vivar, PhD; Brian Smith, PhD, and Andreas M. Beyer, PhD, are on the organizing committee; and Jane Thelaner is coordinating the symposium.

More information is available at www.mcw.edu/Redox-Biology-Program/2018-Symposium.htm.

ATTENTION BIOPHYSICS PERSONNEL

Biophysics Holiday Party

The Biophysics Holiday Party will be held Tues., Dec. 19. Details to follow!

Join Our Club!

Every Friday, members of the Biophysics Hard Roll Club take turns bringing in hard rolls (or bagels, donuts... your choice) to share with other members of the club. If you'd like to partake in this time-honored Biophysics tradition, [email Jane](#).

DEPARTMENT NEWS

Welcome

- Michael Lerch (assistant professor)
- Elizabeth Noey (research scientist)
- Natalia Stein (postdoc, Subczynski lab)

Meet Assistant Professor Lerch

Michael Lerch, PhD, began as assistant professor in the Department of Biophysics in September. His research focuses on defining the molecular mechanisms of protein function, particularly with respect to the functional role of protein conformational heterogeneity.

Dr. Lerch earned his BS in chemistry in 2009 from the USF and his PhD from the UCLA in 2015. His postdoctoral work in Wayne Hubbell’s laboratory at the Stein Eye Institute focused on developing and applying high-pressure EPR techniques for studying the functional role of protein conformation flexibility, and on providing structural insights into the mechanisms of membrane protein function using DEER spectroscopy. Dr. Lerch won the JEOL Prize for best presentation by a student or first-year postdoctoral fellow at the 49th annual international Royal Society of Chemistry EPR Meeting in 2016.



Congratulations

- An upcoming special issue of *Cell Biochemistry and Biophysics* will be devoted the Xth International Workshop on EPR in Biology and Medicine, held in Krakow, Poland, in October 2016. This special issue, of which Dr. Kalyanaraman was guest editor, will include five articles (listed below) by biophysics personnel, including James Anderson, Ted Camenisch, Chang Gang, James Hyde, Balaraman Kalyanaraman, Laxman Mainali, Richard Mett, Joseph Ratke, Robert Strangeway, Karol Subczynski, Jacek Zielonka, and Monika Zielonka.
- [Broadband W-band Rapid Frequency Sweep Considerations for Fourier Transform EPR](#)
- [Cholesterol Bilayer Domains in the Eye Lens Health: A Review](#)
- [Modified Metformin as a More Potent Anticancer Drug: Mitochondrial Inhibition, Redox Signaling, Antiproliferative Effects and Future EPR Studies](#)
- [Recent Developments in the Probes and Assays for Measurement of the Activity of NADPH Oxidases](#)
- [High Cholesterol/Low Cholesterol: Effects in Biological Membranes: A Review](#)
- Neil Hogg: published a [paper in Free Radical Biology and Medicine](#)
- James Hyde & Richard Mett: published a [paper in Journal of Magnetic Resonance](#)
- Candice Klug & Katie Schultz: published a [paper in PLoS One](#)
- Shi-Jiang Li: 25 years of service to MCW

International Collaboration

Zheng Yang, MD, PhD, from the Cognitive and Mental Health Research Center and Beijing Institute of Basic Medical Science in Beijing, China, was a visiting professor in the lab of Shi-Jiang Li for the past two months. The purpose of their international collaboration is to study the mechanisms of human unconsciousness with vegetative status.

Preparing a Successful Grant

A colleague of Dr. Kalyanaraman’s recently shared that, after years of having his grants rejected, unscored, he took a grant writing class and subsequently received three NIH grants. Dr. Kalyanaraman encourages all prospective grant writers to take such a class. Conveniently, the MCW CTIS offers a Methods in Grant Preparation seminar series; visit their [website](#) for details.

Biophysics News is a quarterly MCW departmental newsletter aimed at enhancing departmental engagement through information and good news sharing. Do you have information you’d like to share—news, a photo, a recipe? [Send it to Lydia](#).

RECIPE

Roasted Butternut Squash and Chickpeas with Tahini Dressing

Serves 4

Ingredients

Salad

- 1 medium butternut squash, peeled, seeded, and cut into 1 1/2-inch pieces
- 1 medium garlic clove, minced
- 1/2 teaspoon ground allspice
- 3 tablespoons olive oil
- Salt
- One 15 oz can chickpeas, drained and rinsed
- 1/2 medium red onion, sliced into large pieces
- 1/4 cup coarsely chopped fresh cilantro or parsley

Dressing

- 1 medium garlic clove, finely minced with a pinch of salt
- 1/2 cup lemon juice
- 2 tablespoons well-stirred tahini
- 2 tablespoons water
- 2 tablespoons olive oil

Directions

In a large bowl, combine the squash, onion, garlic, allspice, 2 tablespoons olive oil, and a few pinches of salt. Toss until evenly coated and roast on a baking sheet for 45 minutes, or until brown.

About 15 minutes before the squash and onions are done, toss chickpeas with 1 tablespoon olive oil and roast on a baking sheet until hot.

Meanwhile, make the tahini dressing: In a blender, combine garlic, lemon juice, tahini, water, and olive oil. Taste and adjust the seasoning as needed. Add water as needed to thin it out.

To assemble, combine the squash, onion, chickpeas, and cilantro or parsley in a mixing bowl. Add the tahini dressing to taste and toss carefully; alternately, serve the salad with the dressing on the side. Serve immediately.

Adapted from a [recipe by Smitten Kitchen](#).

BIOPHYSICS NEWS

ABOUT OUR DEPARTMENT

The Department of Biophysics is dedicated to quality in research as well as graduate student and postdoctoral training. Our faculty have a wide range of interests, which can be broadly categorized as EPR and MR (brain imaging and informatics) research.

Meet our primary faculty:

- **Balaraman Kalyanaraman** (Free radicals and mitochondria; cancer bioenergetics; neuroprotective drugs)
- **Bill Antholine** (Metallo antitumor agents; adducts and dynamics of copper complexes; EPR of mixed-valence centers in proteins)
- **Jimmy Feix** (SDSL EPR spectroscopy of peptide–protein interactions, membrane protein structure and dynamics)
- **Neil Hogg** (Biological chemistry of nitric oxide and related species in physiology and pathology; oxidative biology of sickle cell disease)
- **James Hyde, emeritus** (EPR instrumentation; fMRI, fcMRI at high spatial resolution)

• **Candice Klug** (Protein structure and functional dynamics studies using site-directed spin labeling EPR spectroscopy)

• **Shi-Jiang Li** (MRI and data analysis to measure brain function and structural network organizations)

• **Karol Subczynski** (Spin label studies on membrane dynamics and organization; spin label oximetry)

• **Jeannette Vasquez Vivar** (Cell-specific redox mechanisms disrupting normal cellular homeostasis)

Supporting our faculty are our dedicated, highly specialized scientific, engineering, technical, and administrative staff and students.

Each quarter, *Biophysics News* will feature the research of one Biophysics lab group, with the intent of providing readers an opportunity to learn about the exciting research activities ongoing within our department. This first issue features the latest work of Balaraman Kalyanaraman.

SCIENCE FEATURE

REPURPOSING METFORMIN IN CANCER TREATMENT: AN OLD DRUG WITH A NEW POTENTIAL (Balaraman Kalyanaraman)

Emerging research indicates that cancers with mutations in genes encoding proteins of complex I of the mitochondrial electron transport chain are more susceptible to biguanides such as metformin (Met), and that patients whose cancers harbor such mutations may be more sensitive to Met. Met is one of the most widely prescribed drugs in the world for treating type 2 diabetes. Because diabetic patients taking Met show a decreased incidence of pancreatic cancer, many clinical trials now are investigating Met's antitumor effects in various cancers. Met's poor bioavailability and decreased chemotherapeutic efficacy made clear the need for a more effective analog of Met. Using a multidisciplinary collaborative approach involving chemists, biologists, and biophysicists, we discovered that a custom-made analog of Met (known as Mito-Met) is nearly 1,000 times more effective than Met in inhibiting pancreatic cancer cell proliferation and progression. Surprisingly, the key mechanism by which Mito-Met exerts antiproliferative effects in pancreatic cells is through a 100- to 500-fold inhibition of mitochondrial complex I activity. Future studies will use EPR to investigate a similar type of mechanism in other tumor tissues.

This study is funded by an NCI grant and was published in the highly respected [Cancer Research](#) journal. This work was accomplished with the help of Gang Cheng, Jacek Zielonka, Olivier Ouari, Marcos Lopez, Donna McAllister, Kathleen Boyle, Christy Barrios, James Weber, Bryon Johnson, Micael Hardy, and Michael Dwinell.

BIOPHYSICS HAS IMPACTED THE MRI WORLD

In a recent presentation to the Board of Trustees, the Dean highlighted the work of Biophysics (and other MCW) researchers that has had worldwide impact.

One highlight was the publication of the first paper on fMRI (1992) and discovery of resting-state fMRI (1995) by James Hyde's lab, which made neuroimaging a mainstay in mapping brain function and led to President Obama's \$2 billion BRAIN Initiative research program. As an example of the paper's impact on the research field, it has been cited 4,710 times in

the scientific literature. (To put this in perspective, if a paper is cited 1,000 times, it is referred to as a citation classic.)

Another highlight was the research of Shi-Jiang Li's lab into the neuropathological, structural, and functional Alzheimer's disease changes that may begin insidiously, 15–20 years before manifestation of clinical systems. This work will impact the clinical field by furthering the understanding of Alzheimer's disease development, as well as promoting disease prevention and therapeutic approaches.

DEPARTMENT NEWS

WELCOME

- Matthew Fischer (research technologist I, Klug lab)
- Holly Haver (IDP student, Klug lab)
- Piotr Stepień (visiting student, Subczynski lab)
- Elizabeth Wong (volunteer, Li lab)

GOOD-BYE

- Mary Tagliavia (transferred to the Cancer Center)

CONGRATULATIONS

- Bill Antholine: Published a [paper in Journal of American Chemical Society](#).
- Jimmy Feix: Received high praise in student evaluations.
- Andrew Huettnner: Graduated Aug 24; currently employed by GE Healthcare.
- Balaraman Kalyanaraman: The Fall 2016 issue of *MCW Magazine* will feature his pancreatic research, which recently was published in [Cancer Research](#).
- Dan Olson: Advanced to candidacy.
- Nathan Skinner: Winner of a Graduate School Research Poster Session award.
- Jane Thelaner: Promoted to administrative associate.

INTERNATIONAL EPR WORKSHOP

The **10th Internal Workshop on EPR in Biology and Medicine** took place in Krakow, Poland, on Oct 2–6. The workshop was chaired by Balaraman Kalyanaraman, Bruce Freeman (University of Pittsburgh), and Tadeusz Sarna (Jagiellonian University). Organization of the workshop was a collaborative effort among the three institutions. Jane Thelaner, associate assistant, working closely with Jagiellonian University, helped coordinate the event.

Speakers from around the world presented on topics including EPR instrumentation and methodology, metals in biology, distance measurements by site-directed spin labeling, synthesis and use of new spin labels and spin traps, ROS/RNS and oxidative damage, EPR imaging, oximetry, free radicals and excited state species in photobiology, advanced optical imaging, and fluorescence detection.

Speakers from our department include Jimmy Feix, Balaraman Kalyanaraman, Candice Klug, Karol Subczynski, Jeannette Vasquez Vivar, and Jacek Zielonka.

Select photos from the workshop are presented below.



RECIPE

CHRIS FELIX’S WORLD FAMOUS
GROUNDHOG BROWNIES

(contain no actual groundhogs)

- 1½ cups all purpose flour
- ½ teaspoon baking soda
- ½ teaspoon salt
- ⅔ cup butter
- 1½ cups sugar
- 4 tablespoons water
- 2 12-ounce packages Nestle Semi-Sweet Real Chocolate morsels
- 2 teaspoons vanilla extract
- 4 eggs
- ½ cup chopped nuts (optional)

Note: This is a double recipe.

Preheat oven to 325°F. Grease two 8×8-inch baking pans.

In a small bowl, combine flour, baking soda, and salt; set aside. In a small saucepan, combine butter, sugar, and water; bring just to a boil, then remove from heat. Add 12 ounce of chocolate chips and vanilla extract. Stir until chips melt and the mixture is smooth. Transfer to a large bowl. Add eggs, one at a time, beating well after each addition. Gradually blend in flour mixture. Stir in remaining package of chips. Transfer mixture to the baking pans. Add the nuts to one of the pans and stir with knife.

Bake approx. 30–35 minutes. When done, a knife inserted into the pan should come out “clean.”

2016-17 PACKERS
SCHEDULE

- Nov. 6 @ 3:25 pm* - Colts
- Nov. 13 @ 12 pm - Titans
- Nov. 20 @ 7:30 pm - Redskins
- Nov. 28 @ 7:30 pm - Eagles
- Dec. 4 @ 12 pm* - Texans
- Dec. 11 @ 3:25 pm* - Seahawks
- Dec. 18 @ 12 pm - Bears
- Dec. 24 @ 12 pm* - Vikings
- Jan. 1 @ 12 pm - Lions

* at Lambeau Field

