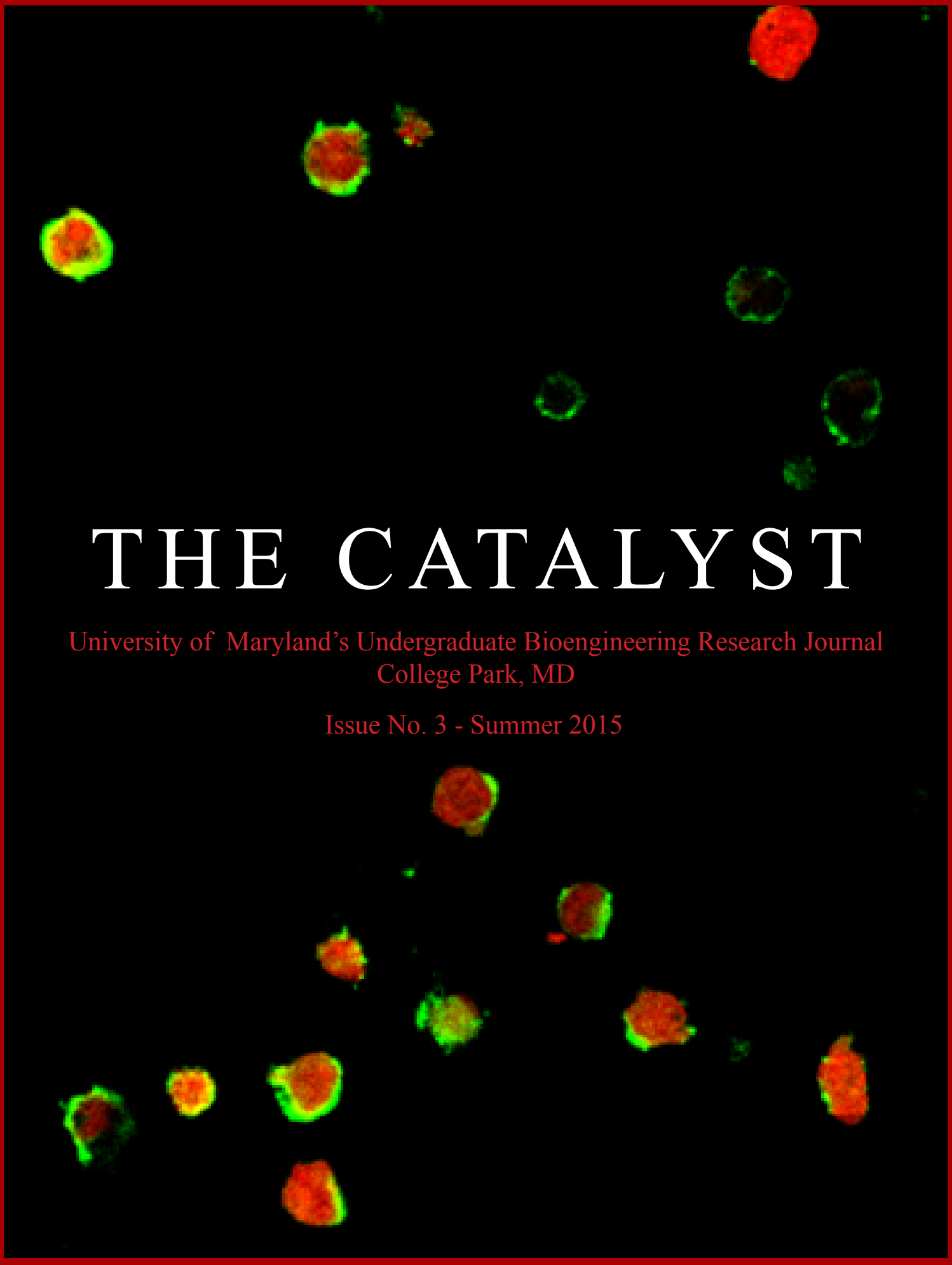

THE CATALYST

University of Maryland's Undergraduate Bioengineering Research Journal
College Park, MD

Issue No. 3 - Summer 2015

Want to get published in the next issue?

THE CATALYST

The Catalyst is UMD's undergraduate bioengineering research journal. We are looking to publish a variety of related undergraduate research with our fourth issue coming this Winter 2016! If you are an undergraduate student working on publishable research related to biomedical engineering and biotechnology, you are qualified to participate. Contact us via email or submit your research abstract through the link provided below. Feel free to check out our previous issues as well.

No research experience?

You can still take part in *The Catalyst's* News Updates sections, which showcases topics such as recent BioE student events. Email us if you are intersted in contributing.

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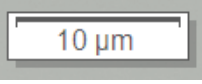


Letter From the Editor

Dear Reader,

The following issue presents the third issue of *The Catalyst*, the first undergraduate bioengineering research journal at University of Maryland. This issue includes research by a BioE undergraduate, an article about this year's UMD-JHU contest, research tips, and a snapshot of the 2015 capstone design competition. In addition, this issue contains interviews with three bioengineering alumni that pursued different pathways after graduation. This issue expands upon the strong foundation that we have laid in previous issues.

I am a graduating bioengineer that joined *The Catalyst* since the first issue that was published in Summer 2014. I grew up in Iran until the age of 16, and moved to Maryland to pursue my college studies in a biomedical field. Passionate engineering students, dedicated faculty, and a well-designed program turned UMD into an outstanding experience for me. As I am moving on to Cornell for graduate studies, I decided to lead *The Catalyst* in my last semester at Maryland and make a difference for our research community.

Our team has been working rigorously to put together a professional work through our student-led organization. The students on our team have contributed numerous hours of work alongside their heavy load of school and extracurricular activities. I would like to give special thanks to Kevin Pineault (former editor-in-chief) who helped me by sharing his invaluable pieces of advice. I would also like to acknowledge the support from Dr. Angela Jones, our faculty advisor, and the bioengineering department.

This semester, The Catalyst took a major step to raise funds to issue paper prints. Although the attempt through LaunchUMD organization was not successful, it laid the cornerstone for future fundraising and collaborations.

Our mission is to galvanize interest in biomedical and biotech research throughout campus. In addition, we wish to foster a more integrated community of researchers within Maryland. Our journal has been successful in providing a medium for students to publish their work, and for faculty to recruit talented researchers in their laboratories. I hope you enjoy reading our third issue.

Sincerely,

Nariman Ziaee

Getting Involved in Research: An Undergraduate's Perspective

By Kevin Pineault, Research Chair

"Why start doing research?" I often get this question from engineering and pre-medical students alike. As a bioengineering major and officer in the Pre-medical Society, I talk to students everyday who are not only interested in the biomedical sciences but also wish to be more competitive for industry jobs, graduate school, and potentially medical school. As you will read in the interviews within this very journal, faculty in the Clark School heavily support undergraduate research and believe the experience can be a profound and productive way of allowing students to independently develop problem-solving skills and learn techniques specific to their field. After graduation, these skills and techniques can prove to be invaluable; they are applicable to a wide variety of jobs and applications.

Undergraduate research is the chance to determine what areas of research are most interesting and exciting for you to learn. Determine what excites you! There will not be many other opportunities when so many laboratories, conducting innovative and unique research, are in such close proximity to one another and are led by faculty dedicated to educating students.

When you realize you want to contribute to work being conducted in a laboratory, I suggest first researching department websites within the University and finding the respective lists of faculty. Look at each faculty member's research interests. Visit and explore their lab website. By reading about past and current projects being completed you can gain insight on the type of projects you would be working on within that area of research.

Talking to upperclassmen during research-related student organization meetings can be very helpful. Stop by a BMES meeting this coming fall! Ask about professors, their research, what work undergraduates have done, and how to successfully publish or apply for grants and scholarships. Graduate student Teaching Assistants (TAs) are also willing to help undergraduates get involved in research. If you are interested, TAs can establish communication between you and their faculty mentor.

After you determine professors you would like to work with, I suggest preparing a short email stating your desire to join the lab as an undergraduate research assistant. You are welcome to shortly describe: why you would like to join (relate to what you read online) and how you could contribute (previous experience or classes related to research projects being conducted). Professors, if interested, will likely ask for additional professional materials and may welcome you to stop by for an interview and walk around their laboratory.

The University of Maryland offers an extensive number of research programs and grants for students interested in conducting research. Here is a quick list relevant to students interested in the biomedical sciences: Maryland Summer Scholars (National Scholarships Office), University of Maryland Scholars Summer Research Program (University of Maryland School of Medicine), Nathan Schnaper Summer Intern Program in Cancer Research, NIH Summer Internship, Howard Hughes Medical Institute Research Fellowship, Godo Biomedical Sciences Scholarship, and ASPIRE Program (MTech).

UMD-JHU Biomedical Engineering Society Undergraduate Research Day Goes Great Despite Snow

By Adam Berger, Design Chair

Started a couple years ago to allow local undergraduate bioengineers to have a chance to present their work, the annual UMD-JHU Biomedical Engineering Undergraduate Research Day was a big success this year. Traditionally, the event has been a friendly competition between the biomedical engineers of JHU and the bioengineers of UMD. Each school can have as many poster presentations as wanted, and they must each select three oral presentations to represent their school. The school that wins first place wins it all. Last year, JHU took home the trophy. UMD wanted to once again win the trophy after winning two years ago. To add a spin to this year's event, the University of Delaware, which recently started a BME program, attended, bringing numerous poster presentations.

The original date planned for the event was March 6th, 2015. Unfortunately, this date was snowed out, so the BMES executive boards moved the date to Friday, March 27th, 2015. This year's event was hosted by JHU in Hodson Hall. UMD brought poster presentations by **Angelina Nou, Erin McCaffrey, Adam Berger, Brian Heligman, Rebecca Stevick, Ariel Isser, Arjun Adapa, William Leverage, Nadia Abutaleb,** and **Havisha Garimella**. BMES-UMD President **Winston Liu**, BMES advisor **Dr. Ian White**, and BioE communications coordinator **Alyssa Wolice** were also present for support. The three UMD oral presentations were "Harnessing Nanotechnology to Design Liposomes to Combat Autoimmunity" by **Arjun Adapa**, "Point-of-Care Biosensors for Hyperammonemia and Aminoacidopathies" by **Brian Heligman**, and "Measuring Cell Traction Forces in Simulated Microgravity" by **Rebecca Stevick**.

The UMD Participants in the BMES-UMD Research Day

A keynote address was given by **Dr. Elliot McVeigh**, a professor and chair for the JHU biomedical engineering department. He talked about his work in medical imaging. His work encompasses using medical imaging techniques, such as MRI and CT scan to visualize the blood vessels surrounding the heart. He provided an example to the undergraduate bioengineers in the audience about how bioengineering research can be applied to the real world.

After the presenters finished and the judges concluded their deliberation, it was time to announce the competition winners. The people's choice poster presentation winner went to **Bretta Fylstra** from the University of Delaware for her poster "A Model to Customize AFO Footplates to Preserve Shank Progression with Limited Ankle Dorsiflexion". Next came the oral presentation winners. From UMD, **Arjun Adapa** won honorable mention. Third place also went to a UMD BioE major, **Rebecca Stevick**. Second place was given to a Materials Engineering major from UMD, **Brian Heligman**. The first place winner was **Andrew Tsai** from JHU for his project "Tunable Electrospun Antimicrobial Coatings for Orthopedic Implants". Although UMD BioE students did not win the trophy, they are sure to come back fighting hard when it is hosted here next year!

Capstone Design Competition 2015

By Nariman Ziaee, Editor-in-Chief with Guest Author Dr. Martha Connelly

Dr. Martha Connolly is the director of bioentrepreneurship, a new program supported by the Maryland Technology Enterprise Institute (Mtech). In addition, she is the class advisor and assists in the instruction of the BIOE 485: Capstone Design course. The following introduction by **Dr. Connolly** addresses the objectives of the BioE Capstone:

> "UMCP's Fischell Department of Bioengineering (BioE) seniors design and build devices meant to improve patient outcomes and improve health care while lowering health care costs.
> In the Capstone course, teams of senior BioE students create their own engineering designs from concept to product, while also learning about market research, the patent process, business plans and ethics. BioE teams are typically matched with a pair of advisors including a member of the BioE faculty and a physician, engineer, or researcher from UMB, or a regional hospital, business, university, or national laboratory. This year, there are 91 students comprising 18 teams of device developers.
>
> At the end of each spring semester (this year it is on May 13th) students, mentors, and guests are invited to a special event at which they can visit exhibits, see demonstrations of biomedical device prototypes, interact with Capstone team members, and learn more about each project's goals, challenges, and results. The event includes the Capstone Design Competition, created and sponsored by **Mrs. Susan Fischell**. A panel of judges selected from industry, national research laboratories and academia rank each project, honoring the best with the First Place and Second Place, and the Patent, Impact, and the Best Business Plan Awards. The seniors select a sixth project to receive the Students' Choice Award."

This year's capstone was comprised of diverse and intellectually challenging projects. Ninety-one students formed 18 groups of five and worked over two semesters to develop and present their products on May 13th, 2015. **Dr. Tao** believes that capstone allows students to "kill multiple birds with one stone" after stepping into industrial or entrepreneurial pathways. Thus, alongside with well-known judges from FDA, NIH, and UMD organizations, he decided to create a "Shark Tank" style competition for the best 5-min business pitches. Capstone teams were judged by primary judges: D**rs. Abbie Sheomaker, Brian Lipford, Zeynep Erim, John Karanian, Jafar Vossoughi**; and also judged by special guests: **Drs. Dean Chang, Kimberly Wallace, Gayatri Varma, Jeffrey Gibbs,** and **David Wise.**

Capstone 2015 at rotunda, located in Kim Engineering Building.

This year's capstone projects delivered their products in the form of devices, computer designs, codes, and medical solutions. A few of the teams, such as team 12 (Biomedical Prophylactic Back Brace), filed a patent for their device, and are currently working on selling the idea to larger companies. National conferences were also a great hub for students to present their capstone ideas prior to the competition day. Team 7 (Locally Sourced Electrolytes for Treatment of Dehydration) participated in the Rice 360 global healthcare competition and received the People's Choice Award. In addition, team 5 (Cardiac Chest Tube Single Incision System) participated in the NEBEC Northeast Bioengineering Conference. This team won the project award for Shark Tank pitch as well. The list of capstone 2015 winners is as follows:

1st Place:
NAP'D: Neonatal Acoustic Protection Device
Louis Born, Erin Kreeger, Makenzie Miller, Siddarth Plakkot, Alyssa Sims

2nd Place:
SensiMatt: A Dynamic Pressure Relieving Medical Mattress
Zack Brandes, Meghan O'Lone, Nitish Malladi, Grace Wang, and Andrew Wesley

Students' Choice:
3D Printed Patient-Specific Pulmonary Models as a Preoperative Method
Brittany Greene, Priyanka Jayanti, Fatemeh Khouzaei, Kelly Leimkuhler, Ashley Matos, Zurana Taluckder

Best Patent:
Portable Stroke Rehabilitation System with Real-time EEG Neurofeedback, Sensory Substitution, and Social Engagement
Anastasiya Belyaeva, Elena Galbally, Vasudha Kowtha, Becky Selle, and Jenny Vojtech

Best in Lean Launchpad Business Model:
Lift-Safe: Preventing Lower-Back Pain in the Workplace
Sean Connolly, Anthony Dinh, Corey Koller, Christopher Meyer, and Gaurav Nayyar

Social Impact Award:
Engineering Locally-Sourced Oral Rehydration Solutions
Chris Cherry, Connie Chen, Hannah Hafez, Dan Hogan, and Nariman Ziaee

Shark Tank: Most Creative Project Award:
Mobile iCP: A Non-invasive Intracranial Pressure Monitor
Nayeem Chowdhury, Carolyn Kleinberger, Hannah Ornstein, Michelle Patkin, Rebecca Stevick

Shark Tank: Best Project Award:
Single Incision Cardiac Chest Tube Housing
Nathan Barber, Julie Etheridge, Alex Jankovic, Chavi Rehani, Michael Sikorski

The grand prize went to team 13, the Neonatal Acoustic Protection Device project. **Siddarth Plakkot,** one of the team members, decided to share the details of their project with us. Team 13 was supervised by the faculty advisor **Dr. Tao**, and the clinical mentor **Dr. Rose M. Viscardi** of the Pediatrics Department at University of Maryland School of Medicine.

As **Siddarth** explained, sensorineural hearing loss is a major risk for infants who remain in the neona-

tal intensive care unit (NICU) for extended periods of time. In fact, 52% of infants who exit the NICU leave with abnormal audiograms. Noise produced by life supporting machines and other sources can result in sound levels reaching as high as 90 dB, which is well above the 45 dB level recommended by the American Academy of Pediatrics. Existing products like the MiniMuff use a hydrogel adhesive that surrounds the infant's ear, but is quite cumbersome and irritating to their skin. Moreover, Minimuff products can only reduce noise levels by approximately 7 dB. Siddarth stated that "our ear-encapsulating cap device uses active noise cancellation technology where noise … is collected by a microphone and sent through a circuit to produce a wave that … cancels the noise." This device is meant to be easily integrated into infant caps that are already in use. The device is a compact, safe, non-irritating alternative that can better attenuate noise levels for infants in the NICU.

Siddarth thinks their project won capstone because it could potentially help solve a clinical need that is often unknown or overlooked, but can be easily addressed. "It was surprising to see that many of those who visited our poster were unaware of the significant sensorineural hearing loss that occurs in infants" he added. Additionally, the market for this device can be expanded to beyond just NICU infants. With the addition of a Bluetooth component in the circuit, this device can provide beneficial audio such as womb sounds, the mother's voice, or classical music to calm the baby, while still reducing excessive noise. Team 13 is currently working with the UMD's Office of Technology Commercialization to pursue a patent.

Team 13, the capstone 2015 first place winners.

This year's capstone was comprised of diverse and innovative projects that impressed the judges. Once again, the Fischell Department of Bioengineering at the University of Maryland illustrated the great outcome of its rigorous program, dedicated faculty, and hardworking students at capstone 2015.

Capstone Team Spotlight

Portable Rehabilitation System with Real-Time EEG Biofeedback and Sensory Augmentation
By Anastasiya Belyaeva, Elena Galbally, Vasudha Kowtha, Becky Selle & Jenny Vojtech, Guest Authors

The RePowered team (left to right): Vasudha, Anastasiya, Jenny, Becky, and Elena

The RePowered team is currently developing a rehabilitation system for those with proprioceptive and mobility impairments, such as stroke patients. The device expands upon current rehabilitation methods, yet combines both portability and biofeedback with a social platform to create a unique and ideal system for at-home rehabilitation. The online platform hosts gamified rehabilitation exercises in the form of simple video games as controlled through a Kinect. Moreover, this social platform allows for interaction with other users as well as a patient's physical therapist. Real-time biofeedback is based on the use of a wristband that vibrates to help guide the patient through gamified reaching tasks and an EEG headset to provide information about. The vibrotactile feedback is utilized as sensory augmentation that additionally allows for the measurement of multiple parameters, such as position and jerk of the arm. Neurofeedback is employed through the EEG headset to train the brain to regain function in the motor cortex.

On the Cover

By Adam Berger, Design Chair

The front cover of this issue is a picture of EoL-1 human eosinophilic leukemia cells treated with Prussian Blue (PB) nanoparticles. The biofunctionalized PB nanoparticles were synthesized and then used to treat the cells. The cells were then fluorescently labeled and imaged using a fluorescnce microscope to get the image seen on the cover. Turn to the full article on page 19 to read more. Reproduced with permission from the American Chemical Society.

Meet the Faculty: Dr. Kimberly Stroka
Strok[a]ing the Surface of Her Research Life

By Dani Mahsan Khalilzadeh, News Chair

Every year, the university provides the opportunity for great researchers with ground-breaking research to open up laboratories that will build up on their respective field of research. This year, one of the newest additions to the University of Maryland's Bioengineering faculty was Dr. Kimberly Stroka. Dr. Stroka has recently opened up the Cell and Microenvironment Laboratory in the Chemical and Nuclear Engineering Building, and she is currently a professor for Biomechanics, a course offered for bioengineering undergraduates. Throughout the scope of this article, we will divulge into the background of exactly who Dr. Stroka is, how she became a well-known published author in the biomechanics/biophysics research field, her advice to students following her career path, and the workload involved with opening up a new laboratory.

Background

Dr. Stroka's interest for research bloomed very early in her academic career. Her experiences and internships throughout her undergraduate years allowed her to find her passion for the field of biophysics. She received her Bachelor's degree in physics from Denison University. While in college, she loved the analytical aspect of physics, but there wasn't a research area in pure physics that she was interested in. Dr. Stroka had always been drawn to the field of biology as well, so while she was in college she sought out opportunities to perform biophysics and other bioengineering-related research.

Her first research opportunity came along when she participated in an NSF-REU summer program at Bucknell University. The next summer, she started her senior honors thesis, where she designed a project that involved biomechanical analysis of the forces acting at the shoulder joint during the pole vault. After graduating from Denison University, Dr. Stroka decided to come to the University of Maryland to pursue a PhD in bioengineering. During her PhD, her work was focused on understanding endothelial cell biomechanics, as well as how white blood cells cross the vascular endothelium during an immune response and cardiovascular diseases.

Soon after earning a PhD, Dr. Stroka began her postdoctoral research in the Chemical and Biomolecular Engineering Department at Johns Hopkins University. Her postdoctoral work focused on understanding different aspects of tumor cell metastasis.

Research

Dr. Stroka's research is extremely interdisciplinary, as it integrates aspects of biology, engineering, materials science, and physics. Since January 2015, Dr. Stroka opened up the Cell and Micro-environment Engineering Lab located in the Chemical and Nuclear Engineering Building. One of the major projects that her lab focuses on is understanding how tumor cells cross the blood-brain barrier during metastasis to the brain.

She mentioned that "in the first phase of the project, [they] are looking at how cues from the micro-environment regulate the integrity of the blood brain barrier during normal conditions, and also how blood-brain barrier function changes in the presence of tumor cells. [Their] goal here is to determine what micro-environmental factors (whether from other nearby neural cells or from the extracellular matrix) affect tumor cell mechanobiology, and in turn, what effects the tumor cells have on the micro-environment." For the second phase of the project, she explained that "[they] aim to engineer a "blood-brain barrier-on-a-chip" which can be used not only to understand fundamental aspects of tumor cell metastasis, but also be used as an alternative to animal models in screening drugs or testing drug delivery mechanisms."

Reasons for Joining the University of Maryland

Since completing her PhD at the University of Maryland, Dr. Stroka has been intrigued by the "energy and enthusiasm" that is spread throughout the University's Bioengineering Department. She believes that people are constantly working hard not just to improve the Department's ranking, but also to make a difference in people's lives; whether by using engineering to contribute to fundamental scientific knowledge, or by creating diagnostic devices for disease, or through professional development.

Laboratory Start-up: Feelings and Emotions

Setting up her very own laboratory has been a lifetime passion. In her interview, she has mentioned that "there was a specific day a few weeks ago when [she] had just received several large pieces of equipment, and walked into [her] lab and thought, 'Wow, this is [my] lab!' " She also intensely emphasized that "more than anything, [she is] grateful for the opportunity to be here as a professor, starting [her] own lab, and to have the ability to pursue whatever research questions [she] and [her] students find interesting." Perhaps the next emotion she would cite is feeling overwhelmed! She mentions that there are so many tasks involved in setting up a lab, including getting quotes from suppliers, ordering equipment and supplies, training students, making decisions about lab renovations, setting up organizational systems within the lab (chemical inventories, safety information, SOPs), and figuring out a budgeting strategy. Despite all of the work that she has ahead of her with regards to operating her lab, she is still thankful for everything that she has acquired and is excited for the long journey she has ahead of her as both a professor and researcher.

Approach to Research

At this point, she prefers to be more hypothesis-driven. However, she has a few ideas for grants that encourage high-risk and high-reward type of research that will encourage her to be more exploratory and adventurous.

Advice to Students

Even though Dr. Stroka has just opened up her own laboratory, she still has a few pieces of advice for people who intend on following in her footsteps.

For PhD students and students who seek careers in academia, she has the following advice:
"(1) Get research experience as an undergraduate, and try to go to at least one conference or get a co-authored paper as an undergraduate
(2) Find a PhD mentor who completely supports your goal of becoming a professor and constantly seek his/her advice
(3) Build a network of other mentors who will also contribute to your scientific and professional development
(4) As a graduate student, take advantage of as many opportunities as possible, including going to conferences, writing fellowship applications, applying for awards, collaborating on projects, etc. These will not only build your CV and give you momentum down the academia path, but will also provide you with invaluable experiences that you can draw on along the way."

She also has valuable advice for undergraduates who are just beginning their journey as researchers:

"Try to figure out what you love to do. If you think you might enjoy research, join a lab early in your undergraduate career and try to get something tangible out of it (a paper, a presentation at a conference, etc.). If you are interested in industry, apply to do an internship over the summer. If you're interested in entrepreneurship, talk to a professor in the department about how you can learn more about that process. Be proactive, and get out there and talk to people."

Daily Life

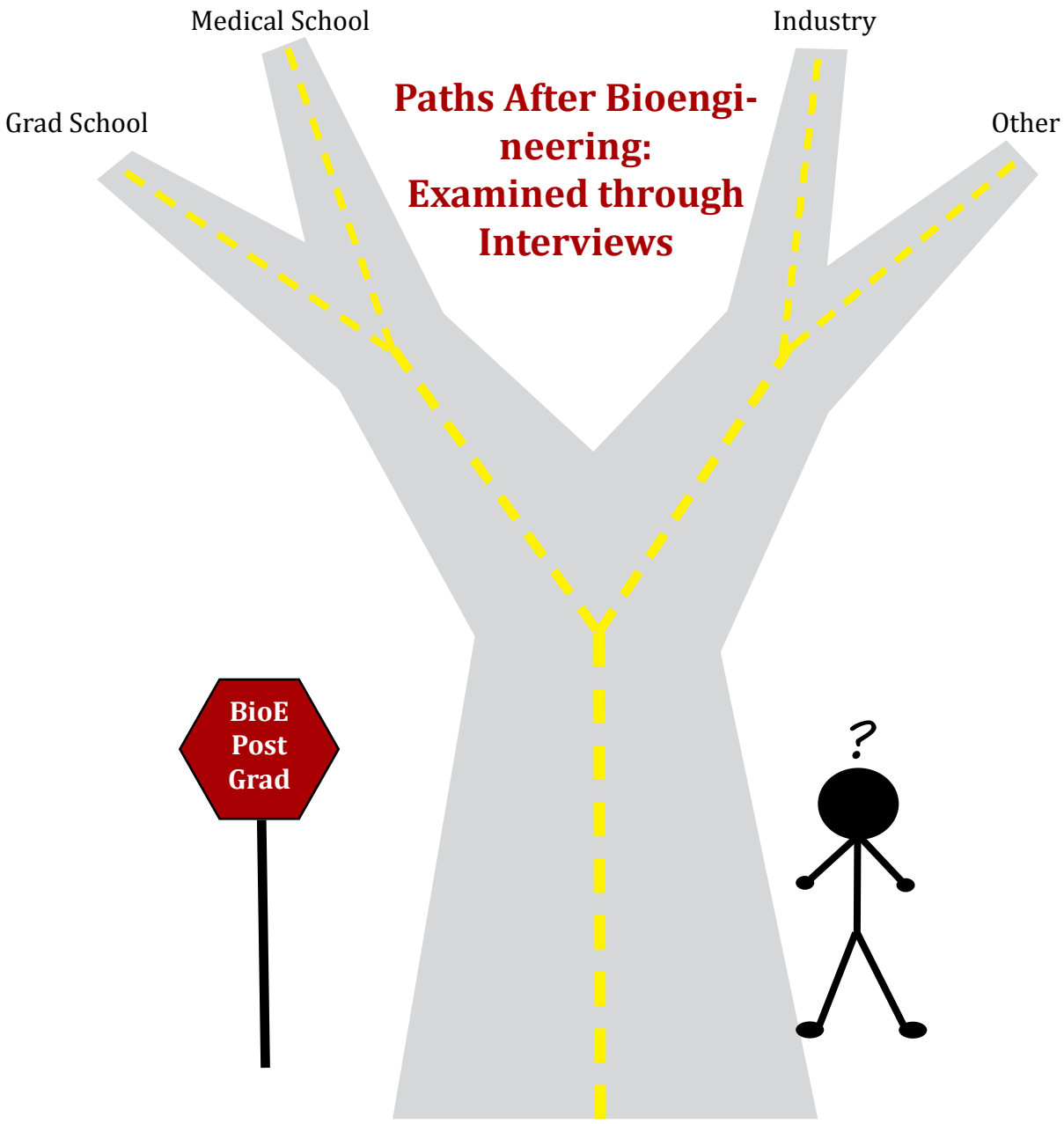
Daily life as a UMD Bioengineering professor is "busy"! In her own words, Dr. Stroka claims that "there are so many aspects to life as a professor, and it is challenging to balance it all." She notes that each component (research, teaching, service) could probably be a complete job in itself and that the challenge is trying to get everything done while still maximizing performance in each area. Not only is Dr. Stroka a researcher, but she is also a professor here at the University of Maryland. She is currently teaching Biomechanics and notes that teaching a course for the first time is a lot of work, but she is anticipating that this will become much easier in subsequent semesters when she teaches the same course again. Building and managing a lab is also a lot of work, but she feels fortunate to have recruited 2 excellent PhD students and 4 enthusiastic undergraduates who are willing to start this journey with her. Dr. Stroka also has committed to balancing her work life with family life. She is married and has a 12-month-old baby, so she makes it a priority to spend quality time with her family.

Acknowledgements

Dr. Stroka would like to give a special shout-out to all of her fantastic mentors that have helped, supported, and mentored her throughout all of the stages in her career. She is also thankful to the Fischell Department of Bioengineering for providing her with her current position along with continual support for her career. She is extremely excited to start her own lab and to have the ability to pursue whatever research questions she and her students find interesting.

End Note

All in all, we are so excited to have Dr. Stroka join the Bioengineering faculty here at the University of Maryland. As she embarks on her new journey, we cannot wait to follow up on her groundbreaking research and to use her experiences and advice throughout our own academic/research careers. As an individual who has been a member of her lab since it has started, I can vouch that she has been an inspiring mentor who has increased my thirst for knowledge on biophysics (e.g. tumor cell metastasis) research, and I cannot wait to see what other interesting research she has in store for me as I begin my undergraduate bioengineering honors research thesis.



Graduate School

by Nariman Ziaee, Editor-in-Chief

David Peeler is a former student of UMD Bioengineering He was the president of UMD's BMES chapter while at UMD from 2009-2013. He is currently a first year doctoral student in the Department of Bioengineering at the University of Washington, developing nano-biomaterials for targeted delivery of drugs and biologics. In the year prior to moving to Seattle, he conducted research on the antimicrobial efficacy and biocompatibility of silver nanoparticles at FDA in White Oak. He talked to *The Catalyst* about what it is like to pursue grad school after bioengineering.

Why did you choosethe grad school pathway? What was your undergraduate experience that prepared you for it?

"When I applied to UMD, I thought that I would use my B.S. in Bioengineering to give me a competitive edge over general biology majors when applying to medical school, and perhaps I would learn something great along the way. I also knew that I wasn't going to settle for an entry level job and that I would need an advanced degree to be a manager (as opposed to the managed) in my future career. The factors

that pushed me beyond this state took place over the course of several years, and may be boiled down to three things:
1) Fascination: I realized that biomaterials was an area that allowed me to design materials using chemistry (my favorite basic science) with the potential for huge impact in medical applications. While physicians treat many patients over their lifetime, a bioengineer can impact thousands or millions of lives at once.
2) Experience: Before getting my first internship, I spent time talking to professors and physicians to figure out what their lives were like and what it would take to be like them. The process of asking for advice has never stopped and never will—you absolutely have to be curious in order to find out what the world is like and how you fit into it. Nevertheless, it wasn't until I spent a year and a half in Dr. Matysiak's Biomolecular Modeling Lab that I understood what "researching" was.
3) Quality of life: Medical school will put you deeply in debt, a Ph.D. program will pay you to learn. I do not care about making hundreds of grand. but I want a stable job with reasonable hours. These things are not much easier to come by through a research-based job, but they are more easily achievable."

What is your advice to undergrads?
"Talk to your own and other people's advisors. Also, talk to a current graduate student if you want to have a chance of succeeding in life with your diploma in hand. You have to keep your grades up! However try not to go for a 4.0 GPA. I've been told many times that everything from 3.5-3.8 is regarded as the same and that only a 3.9 or 4.0 will give you bonus points. Meaningful scientific contributions through research are of utmost importance, but meaningful contribution to your community through leadership positions in extracurricular organizations are also important. Above all, my advice is to figure out your skillset and then focus on finding a job that exploits those skills. You most enjoy while you have a balanced life filled with fun and fulfilment outside of work. Do not sell out your intellectual abilities or moral commitments for money—you will be miserable. Do not pick a job because your parents or anybody else wants you to. More specifically, if you do decide to go to graduate school, make every effort to get involved in research that you can, and focus on the transferrable skills you acquire in everything you are involved in. Don't forget that you can seize more opportunities through the magic of relentless and fearless networking!"

What is different about grad school compared to undergraduate?
"Since I talked to many grad students and professors before entering grad school, I haven't been surprised at all. Coursework varies by program/university, but is generally more liberal and strictly tailored to your interests than a set curriculum. Research responsibilities lie more heavily on your shoulders (experimental design and rationale) and less is handed to you. The process is gradual and a thesis advisor should be picked that reciprocates the intensity level of mentorship you desire."

What is your future plan?
"I plan to shoot for a post-doctoral position in academia or at a private research center. In that case, I can research something that excites me with freedom of choice I can manage. I plan to shoot for academia so that even if I miss biotech companies, I will land somewhere nice."

"I could possibly help even more people by making things for physicians to use than by being a physician myself .... money doesn't matter and shouldn't guide your decisions." - David Peeler

Medical School

By Haig Pakhchanian, Staff Contributor

Katherine Chen is a former student of UMD Bioengineering and a current medical student at University of Pittsburgh. While at UMD, Katherine was both an undergraduate researcher and a TA. *The Catalyst* interviewed her to find out what it was like to transition from bioengineering to medical school.

What inspired you to pursue a career in medicine?

"When I first wanted to go into medicine, I had no idea what I was talking about. As a naïve freshman in bioengineering, my ideas of being a physician were superficial at best and absent at worst. I was one of those people who merely "liked science and wanted to help people." Ew, I know. Yet as cringe-worthy as that initial thought was, it was my first step onto the path of exploring medicine.

The most helpful experiences were, unsurprisingly, the ones closest to the field of medicine I was so supposedly interested in. There's a reason schools look for things like shadowing or volunteering when you apply, and it's because they help you understand what you're really getting into with medicine. I learned so much just by observing and talking to people in medical settings. I found I loved the openness and trust of doctor-patient relationships, and I really respected the complexities of the medical decision-making process. Overall, my favorite part was listening to patients tell their stories, or as one doctor more bluntly put it, 'You have to be okay with hearing people complain about their problems every day.'

When I was deciding on applying to medical school, I considered other options. Still, I couldn't see myself working in a lab or in a cubicle 10 years from now, and the more I understood about being a physician, the more I wanted to be one myself. There's so much further to go still. Even now as a first-year med student, I almost feel like a bright-eyed freshman Terp again, wondering if I really know anything about medicine. Slowly though, I've found myself graduating from the observer in the corner to the person in the white coat, listening to real patients 'complain about their problems.' Every day feels like one step closer to actually being able to treat people, and I know there's nothing else I'd rather be pursuing."

What fields of medicine are you interested in?

"It changes all the time - like, every day. Coming in, I think the only thing I ruled out was surgery: not because I was afraid of doing surgeries, but because I was worried the lifestyle was too hectic. Last month, I shadowed an amazing surgeon that does reconstructions for women recovering from breast cancer procedures, and I enjoyed it so much I'm not sure I can even rule out surgery anymore. There's still plenty of time for me to decide though, so I'm not too worried. Plus, they say that you can't really know what specialty you like until you've tried it."

How has your degree in bioengineering helped your approach to medicine?

"There are a couple of other BioE's in my med school class, and I think the common trait that we bring is that we're all naturally curious about the science behind the medicine. At the University of Pittsburgh especially, there's a lot of emphasis on research and new developments in technology and procedures. Coming from bioengineering, that's nothing new to us! The senior capstone project is a pretty great example of how we're always thinking about ways to make things better. Same goes for medicine. The whole idea of evidence-based medicine is that it's important to question common practices until they've been proven to be the best."

During your undergraduate career, what opportunities were you involved in that helped with your pursuit to medical school?
"Research was something I really got into during undergrad, and it became a big part of my application. At UMD, I worked in Dr. Shapiro's lab on nanoparticle characterization for some time, and I also spent a few summers at NIH with MRI and computational biology. Having some experiences with research helps show your scientific curiosity and that you're willing to commit yourself to the process of research. Your mentor can also help write a letter of recommendation for you, which is great because they'll probably be getting to know you well! Other than research, I had some amazing experiences tutoring and TAing at UMD, and I even got to talk about my bioengineering capstone project at one of my interviews."

Compared to other medical students from other universities, do you feel that you were well prepared studying at the University of Maryland?
"Medical school is a whole new game in terms of studying and learning. No matter what major you're in or what school you come from, you have be fully self-motivated in adjusting to med school life because the amount of information you're expected to learn is like nothing before. In that sense, it's like an even playing field, and everyone in your class is struggling right alongside you. Possibly one of the most important skills I learned at UMD was balancing my time with work and play. With all the UMD events popping up on my newsfeed daily, it was impossible not to close my textbooks every once in a while and go out. If I didn't know how to keep myself sane with activities and friends, I feel like I'd end up burning out much quicker."

Looking back at your time at UMD, is there anything that you would have done differently?
"I would have made room for more classes outside my major. There isn't a better time to explore other interesting subjects than undergrad, especially if medicine is in your future. Even down the road when I've forgotten every single partial differential equation I ever learned, I'll still remember how awesome taking West African dance was."

Do you have any other advice for bioengineering students who are interested in applying to medical school?
"Take some time to be really introspective and figure out who you are. Figure out if medicine is really worthwhile to you and fits your personality well, then try your best to get as many exposures to the medical field as you can! Bioengineering is a tough major to juggle a lot of outside commitments with, so don't overextend yourself. Take time to grow, and learn to get along with everyone, especially since you'll see your med school class all the time for the first two years at least. Throughout the application process, keep your sense of humor, don't do anything stupid (no setting testudo on fire!!), and talk to people for advice. No matter what happens, things will work out one way or another."

Industry Before Graduate School

By Haig Pakhchanian, Staff Contributor

Apoorv Gupta is a former student of UMD Bioengineering. After graduation, Apoorv became an Application Development Engineer at Dow Chemical Company. Currently, he is a graduate student at the Massachusetts Institute of Technology. While at UMD, Apoorv was a member of Dr. Bentley's lab.

What has motivated you to pursue research in metabolic engineering?
"When I had first heard of this field, I was honestly just fascinated by its name! I started reading about it more, especially during my time in the Bentley lab. I realized that a lot of tools that we were developing

had applications in metabolic engineering and improvement of production processes. I have also always leaned more towards applied and industrially relevant research, and metabolic engineering seemed to fill those interests well."

What areas of bioengineering are you interested in?
"My interests in bioengineering involve combining ideas from multiple fields. I am especially interested in the interface of device engineering and biology. A lot of research efforts have recently focused on utilizing devices (mechanical and genetic) to high-throughput and large scale platforms for screening libraries of strains and then optimizing them for production. Constructing and automating such platforms is one of the most interesting areas!"

During your undergraduate career, what opportunities were you involved in that helped with your pursuit to graduate school?
"During my undergraduate career, I really just followed my interests very soundly. I gave a special effort to become extensively involved in research. I started early in my undergraduate career so I could have ample time over the years to develop research skills and credentials that I could not have received in the classroom. It also allowed me to build relationships with my lab members and faculty advisor, and to gain a level of independence. As I was also involved in industrially-relevant work, I took summer opportunities to intern at various companies to gain exposure of the industry world. This really shaped my interest and perspective on graduate school by allowing me to gain specific motivation for going to graduate school. I tried to follow a few activities, but become extensively involved in each of them."

How have your experiences working in Dr. Bentley's lab and the Dow Chemical Company helped you with your future?
"My research experiences in the Bentley lab and outside have helped to gain an appreciation and perspective on research. It has allowed me to understand what kind of technologies are at the cutting-edge now and how one should go about pursuing them. It also instilled a spirit of teamwork in me because I realized that research is often best done in collaboration; this is one of the most important and often most overlooked facts about research. I was fortunate enough to have team-oriented environments in all my experiences."

Looking back at your time at UMD, is there anything that you would have done differently?
"I wish I had tried a few things that were completely outside my field, such as a literature club. I also wish I had traveled more than I did. It's only after you graduate that you realize how many more experiences you could have had."

What are your plans after you earn your PhD?
"It's an open question at the moment. I am certainly aiming for industry, however, I am still working out the the details of what kind of role I would like to work in."

Do you have any other advice for undergraduates who are interested in applying to graduate school?
"Work hard during your undergraduate career (not just in your classes) because you only get one shot at college. Explore as many of your interests as you can, but make sure to have a definite direction throughout your years so that when you come out, you have a portfolio with a theme you can present to your future graduate program."

Jenny Vojtech

Jenny has just finished her senior year in the Bioengineering program. Prior to graduation, Jenny spent a year working at the U.S. Food and Drug Administration as a part of the Controlled Substances Staff. Following this experience, she began research at the nearby Children's National Medical Center, where her research focused on theranostics (therapy + diagnostics) using nanoparticles. Within the University, Jenny was a member of the College Park Scholars: Life Science program, in addition to leading Engineering World Health. In her free time, she enjoys hiking, drawing, programming and circuit design, playing with EEG headsets, and spoiling her cat. She will be pursuing a Ph.D. in Biomedical Engineering at Boston University in the upcoming Fall with a focus in signal processing and computational methods.

ABSTRACT

Molecular imaging is useful for the visualization of physiological processes in living specimens. The present study proposes biofunctionalized Prussian blue nanoparticles (PB NPs) for use as an innovative class of molecular imaging agents. Prussian blue is ideal as it is established as an FDA-approved agent for human oral consumption and may be synthesized using a one-pot synthesis scheme. The PB NPs are utilized in fluorescence and magnetic resonance imaging (MRI) to enable visualization of biological processes at cellular- and molecular-level resolutions. Biologically active cations were incorporated into the PB NPs to generate MRI contrast. A fluorescent coating was then added to the particles to enable fluorescence imaging. The particles were then modified with various ligands to enable molecular targeting capabilities. Stability and cytotoxicity of the particles were analyzed, followed by MRI relaxivities. Molecular imaging capabilities were successfully demonstrated through the use of fluorescence and molecular MRI *in vitro*. PB NPs are novel imaging agents that ultimately serve to enhance theranostic efficiency *in vivo*.

Biofunctionalized Prussian Blue Nanoparticles as Multimodal, Molecular Imaging Agents

Jenny Vojtech[1,2] and Rohan Fernandes, Ph.D.[1,2]
[1]Fischell Department of Bioengineering, University of Maryland, College Park, MD; [2]The Sheikh Zayed Institute for Pediatric Surgical Innovation, Children's National Medical Center, Washington D.C.

1. Introduction

Molecular imaging is used to visualize biological processes at the cellular, subcellular, and molecular levels[1]. Specific molecular imaging modalities include magnetic resonance imaging (MRI), computed tomography (CT), fluorescence and ultrasound, among others[2]. These modalities typically allow for a living specimen to remain in its native environment while its various physiological processes are examined. Multimodal molecular imaging combines two or more of these molecular imaging modalities to enhance the visualization of the specimen's biological processes. This enhancement is derived from the complementary features of each modality. In this manner, it is possible to harness the strengths of the individual techniques, while counteracting or compensating for their limitations[3].

We propose Prussian blue nanoparticles (PB NPs) as one multimodal molecular imaging agent. PB is an FDA-approved pigment that is described by a face-centered cubic lattice structure, composed of repeating Fe(II)-CN-Fe(III) linkages (Figure 1)[4]. The interstitial spaces between these linkages allow for the incorporation of cations to balance charges of the lattice network. Additionally, the PB NP core may be coated with biofunctionalized fluorescence particles for targeting. Moreover, the incorporation of biologically active cations such as gadolinium or manganese enables MRI contrast. Similarly, the introduction of a fluorescent coating onto the nanoparticles serves to enable fluorescence imaging. The ability to customize these nanoparticles in such a manner is very desirable for imaging diagnosis. In this manner, the particles may be adapted for various uses. Most importantly, the non-invasive nature of fluorescence and MRI modalities is favorable for imaging diagnosis in pediatrics.

The PB NP core is coated with a shell of the fluorescently-labeled avidin. Avidin is a glycoprotein that is often found in egg white. The addition of the biofunctional fluorescent-avidin shell not only enables fluorescence imaging capabilities, but also

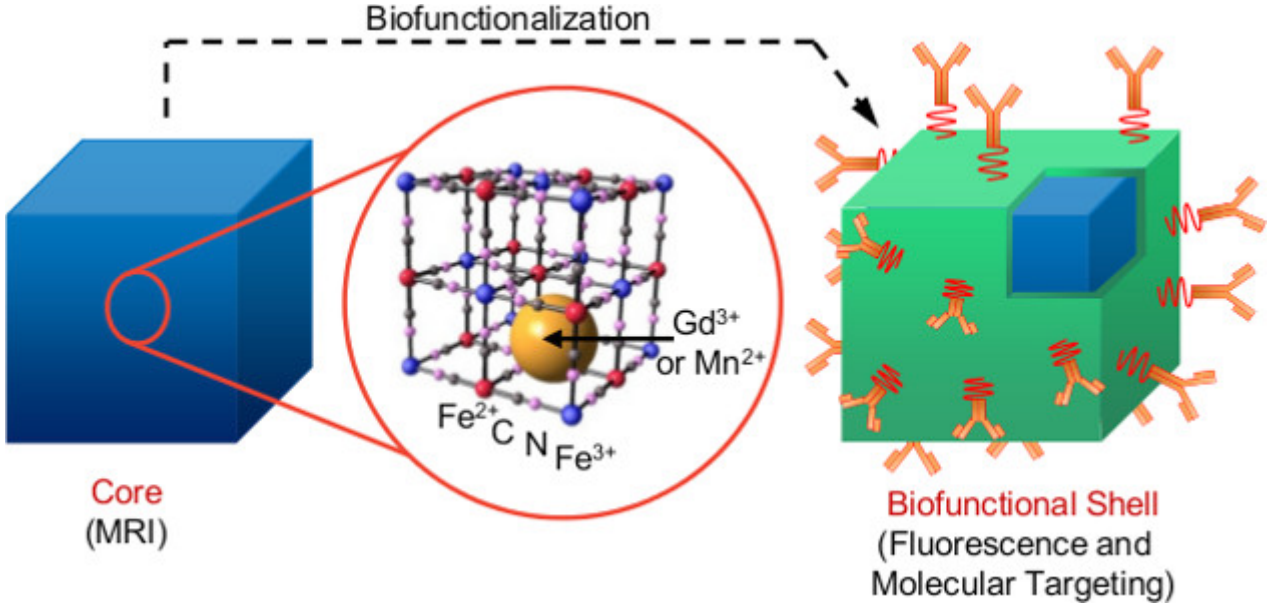


Figure 1. Schematic of Prussian blue nanoparticles, featuring their core-shell design and biofunctionalized coating. The green shell corresponds to a fluorescently-labeled avidin coating on the particles while the numerous "Y" shapes correspond to biotinylated antibodies[4].

presents itself as a platform for biotinylated ligands to target and trace various specific cells and tissues in the body. The ability of avidin to serve as a dock for these ligands is due to the non-covalent avidin-biotin bond, one of the strong bonds known[5].

The present study describes the methods for the synthesis and biofunctionalization of PB NPs, gadolinium-containing PB NPs (GdPB), and manganese-containing PB NPs (MnPB)[6-8]. Size, charge, and temporal stability are measured, followed by an evaluation of the toxicity of the particles. The PB NPs are then demonstrated as multimodal, molecular imaging agents in fluorescence and molecular MR imaging of a population of cells *in vitro*.

2. Methods

The development and analysis of these PB NPs occurred in five major steps: 1) Synthesis and Biofunctionalization, 2) Sizing, Zeta Potential, and Temporal Stability, 3) Cytotoxicity, 4) Measurement of MRI Relaxivities, 5) Fluorescent Labeling and Generation of MRI Contrast on Targeted Cells.

2.1. Synthesis and Biofunctionalization

Synthesis of PB NPs occurred using a one-pot synthesis. A one-pot synthesis scheme allows for the different components that make up the nanoparticles to react through a series of chemical reactions within only one reactor. Gadolinium and manganese cations were incorporated during the one-pot synthesis in order to enable positive and negative MRI contrast. With multiple gadolinium ions incorporated into the PB lattice, signal intensity is greatly enhanced compared to the majority of FDA-approved gadolinium chelate contrast agents that provide low signal intensity [2, 9-12]. Manganese may be loaded into the interstitial spaces of the nanoparticles as a safer alternative to gadolinium, which has been linked to nephrogenic systemic fibrosis [11, 13-14].

Following, biofunctionalization was achieved by coating the "core" of the nanoparticles (i.e. the lattice structure, Figure 1) with fluorescently-labeled avidin. Avidin is a glycoprotein that is often found in egg white. The addition of the biofunctional fluorescent-avidin shell not only enables fluorescence imaging capabilities, but also presents itself as a platform for biotinylated ligands to target and trace various specific cells and tissues in the body. The ability of avidin to serve as a dock for these ligands is due to the non-covalent avidin-biotin bond, one of the strongest bonds known[5]. Biotinylated ligands, such as antibodies, were then attached to the avidin to achieve targeting capabilities.

2.2. Sizing, Zeta Potential, and Temporal Stability

Sizing, zeta potential, and temporal stability are individual studies necessary to characterize the PB NPs. These studies were conducted using dynamic light scattering (DLS) methods that demonstrate overall stability and practicality of the nanoparticles. Sizing was approximated through the measurement of the hydrodynamic diameter of the particles. This diameter is that of the apparent dynamic particle in water (hydrated). Moreover, zeta potential measures the electrostatic charges on the surface of the particles (repulsive and attractive) and was utilized to further ensure stability and characterize electrochemical equilibrium. To determine temporal stability the hydrodynamic diameter of the particles over a span of time was measured to ensure that the particles were stable instead of aggregating, bleaching, or falling out of solution.

2.3. Cytotoxicity

Toxicity of the NPs was measured using an XTT cell proliferation assay over a span of two days. This assay is necessary to ensure that the NPs are not toxic to cells before their implementation in animal studies. Specific cell lines studied were Neuro2a, BSG D10, EoL-1, and OE21. Neuro2a and BSG D10 cells are described as neuroblastoma cell lines extracted from mice. EoL-1 cells are characterized as a human eosinophilic cell (white blood cell) line. Finally, OE21 are described as being a cell line of human Caucasian oesophageal squamous cell carcinoma.

2.4. Measurement of MRI Relaxivities

MRI relaxivities describe the relaxation rate of a sample as a function of concentration. MRI relaxivities of PB, GdPB, and MnPB NPs were measured using T1- and T2-weighted sequences. T1-weighted sequences measure longitudinal relaxation time, while T2-weighted sequences measure transverse

relaxation time. These sequences were analyzed in an MRI "phantom," or well plate filled with various concentrations of samples. Signal intensity of the samples were measured using ImageJ[15]. Regression of the signal intensities and inversion times was conducted using Origin[16].

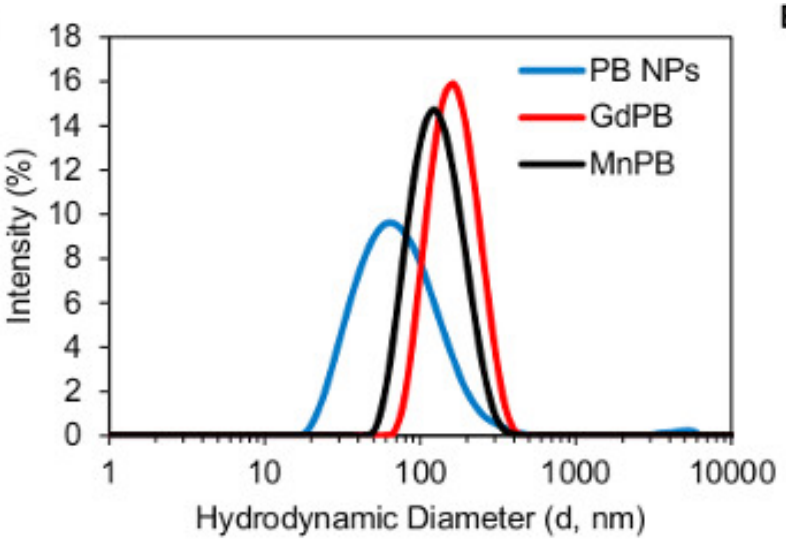
2.5. Fluorescent Labeling and Generation of MRI Contrast on Targeted Cells

Biofunctionalized PB, GdPB, and MnPB NPs are capable of fluorescently labeling a targeted population of cells. This was successfully demonstrated using confocal microscopy and flow cytometry (Figure 4). Confocal microscopy and flow cytometry both detect fluorescence light emissions to distinguish cells and particles. Additionally, the biofunctionalized particles were also able to generate MRI contrast in a targeted population of cells in T1- and T2-weighted sequences by adding cells to a well plate containing various concentrations of the particles. Post-acquisition processing occurred by measuring signal intensity of each sample through the using of the freeware, ImageJ.

3. Results

The one-pot synthesis scheme is an efficient way to generate consistently monodispersed PB, GdPB, and MnPB NPs, as indicated by a monomodal hy-

A



B

Sample	Zeta Potential (mV)
PB NPs	-36.40
GdPB	-32.10
MnPB	-38.83

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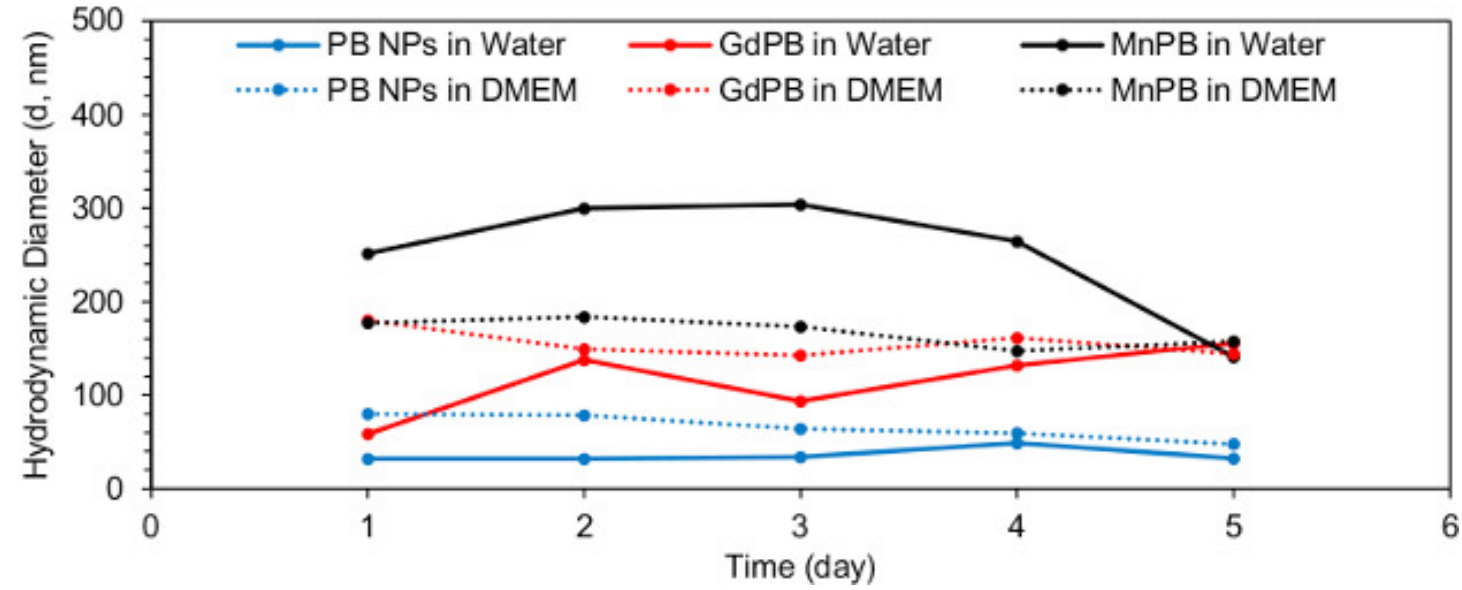
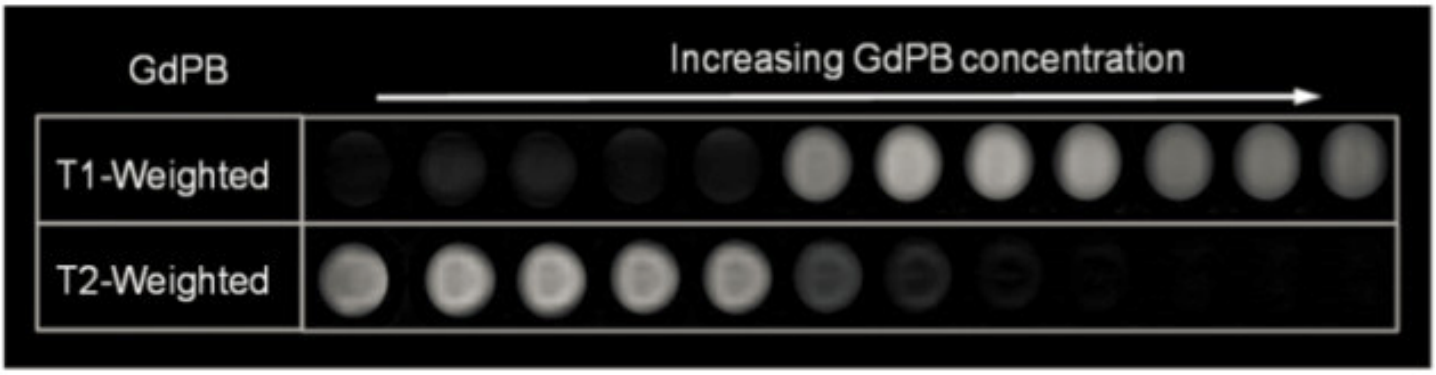


Figure 2. Size, charge, and stability of the Prussian blue nanoparticles. A) Approximate size (hydrodynamic diameter, nm) of each nanoparticle sample, as measured by DLS. B) Zeta potential of each nanoparticle sample, as measured by DLS. C) Stability of the nanoparticles in water and cell media (DMEM) over a period of five days[4].

drodynamic diameter distribution (Figure 2A). The mean diameters were: 1) PB = 78.8 nm, 2) GdPB = 164.2 nm, and 3) MnPB = 122.4 (Figure 2A). The zeta potentials of the nanoparticles were each less than -30 mV, indicating moderate stability of the particles (Figure 2B). A negative zeta potential less than -10 mV suggests stability of the particles. This is due to the negative charges that should surround the positively-charged particles, if synthesized correctly (see Figure 1 to view positive charges). The nanoparticles exhibited adequate temporal stability over a span of five days, as indicated by consistent hydrodynamic diameters (Figure 2C). This temporal stability is demonstrated by the relatively unchanging size of the particles over the span of five days, which suggests little aggregation or destruction of the particles. When co-incubated with cells, the nanoparticles exhibited negligible cytotoxicity on Neuro2a, BSG 10, Eol-1, and OE21 cell lines (see reference 4 for this data)[4].

MRI relaxivity studies indicate that GdPB and MnPB NPs function as MRI contrast agents in both

A



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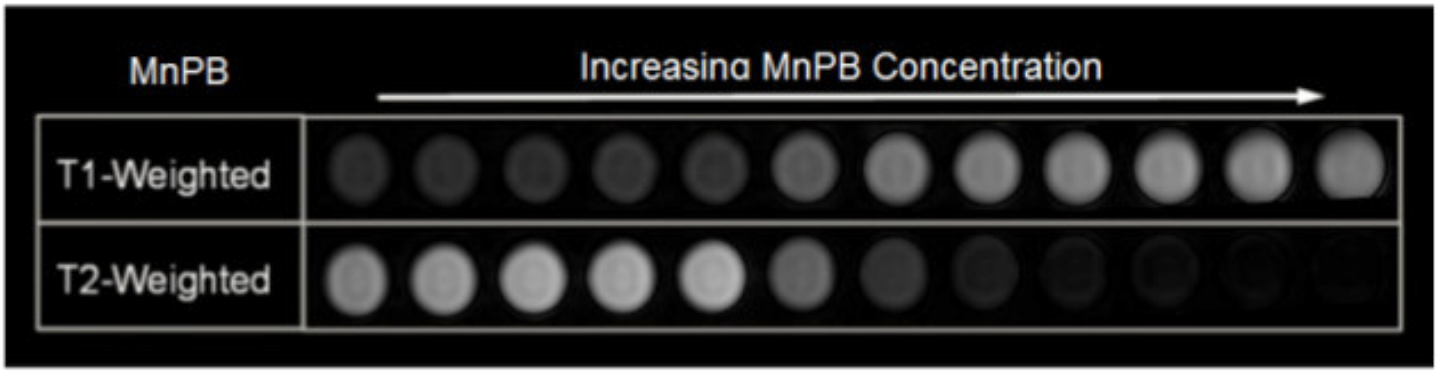

C

Contrast Agent	Relaxivity ($mM^{-1} s^{-1}$)	
	r_1	r_2
PB NPs	7.9	14.4
GdPB	38.5	44.7
MnPB	15.8	143.0

Figure 3. MR images and relaxivities of GdPB and MnPB without cells. A) Positive and negative contrast of GdPB nanoparticles with increasing concentration. B) Positive and negative contrast of MnPB nanoparticles with increasing concentration. C) Measured relaxivities for Prussian blue nanoparticles in T1- and T2-weighted sequences. Reproduced with permission from Ref 14, copyright 2014 American Chemical Society.

T1- and T2-weighted sequences (Figure 3) [11, 14]. This is demonstrated by increased positive contrast in T1-weighted sequences and increased negative contrast in T2-weighted sequences with increasing concentrations of both GdPB and MnPB. The measured relaxivities of GdPB and MnPB are favorable when compared to current clinically approved contrast agents [12-14].

Biofunctionalized PB NPs are capable of fluorescently targeting a population of cells, as demonstrated by flow cytometry and confocal microscopy. Specifically, confocal microscopy demonstrates the presence of nanoparticles in experimental groups (B, D, and F; fluorescently-labeled avidin appears green), with the absence of nanoparticles in control groups (A, C, and E). Panel B utilizes Eot3 as an antibody, which is biotinylated anti-human eotaxin-3.

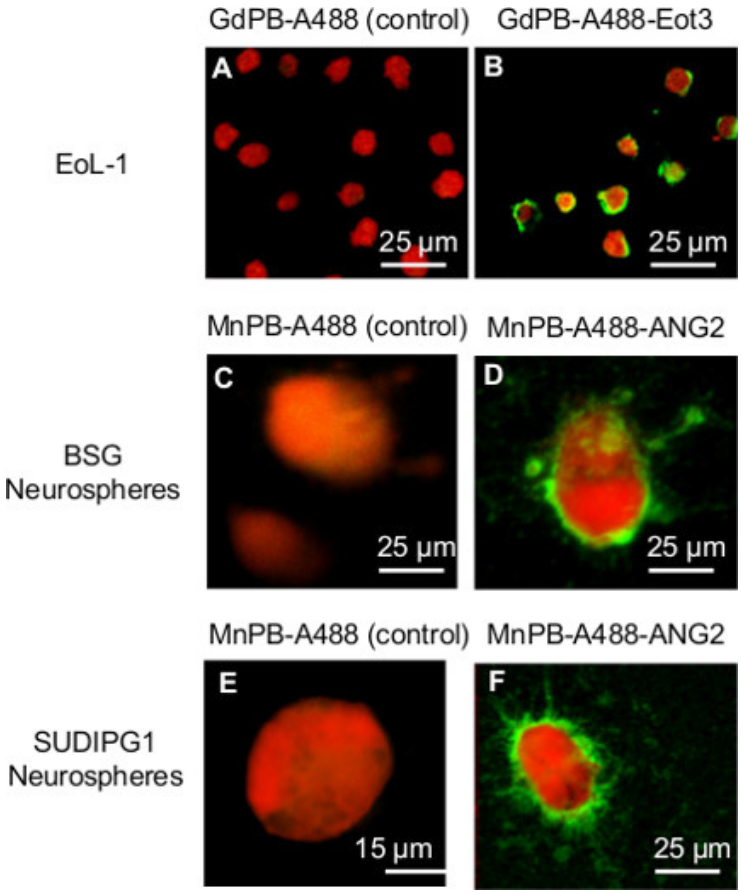

Figure 4. Fluorescent labeling of treated cells using biofunctionalized Prussian blue nanoparticles. EoL-1 cells are treated with (A) control (GdPB-A488) and (B) experimental (GdPB-A488-Eot3) nanoparticles. BSG neurospheres are treated with (C) control (MnPB-A488) and (D) experimental (MnPB-488-ANG2) nanoparticles. SUDIPG1 neurospheres are treated with (E) control (MnPB-A488) and (F) experimental (MnPB-A488-ANG2) nanoparticles. Reproduced with permission from Ref 14, copyright 2014 American Chemical Society.

Eot3 targets receptors that are overexpressed on eosinophils or eosinophilic cell lines, such as EoL-1. Panels D and F use ANG2 as an antibody, which is biotinylated anti-neuron-glial antigen 2. ANG2 targets NG2 overexpressed within cells and tissues of the central nervous system, such as is within BSG and SUDIPG1 neurospheres. These antibodies are specific to the cell lines used. Additionally, the biofunctionalized PB NPs increase MRI contrast in a population of targeted cells when compared to controls.

4. Conclusions

This article presents an overview for the synthesis of biofunctionalized Prussian blue nanoparticles. These nanoparticles are a novel class of multimodal, molecular imaging agents that use fluorescence and magnetic resonance imaging for the non-invasive visualization of physiological processes. The customizability and non-invasive nature of these nanoparticles makes them desirable for pediatric use.

Synthesis of these biofunctionalized PB NPs may be further modified for molecular imaging studies *in vivo*. This modification consists of synthesizing particles capable of being stable in conditions that mimic the human body. This requires tweaking conditions such as pH and temperature that the particles may be stable in. Further studies include the biofunctionalized nanoparticles for use in theranostic (simultaneous **thera**py + diag**nostic**) applications *in vivo*[4].

5. Social Implications

Biofunctionalized Prussian blue nanoparticles are currently being developed for theranostic applications in pediatric cancers and inflammatory diseases. The use of these PB NPs may facilitate diagnosis of these illnesses and provide insight into a proper route of treatment. The customizability and non-invasive nature of the PB NPs makes them desirable for use in pediatric medicine.

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