BIOGRAPHICAL SKETCH

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NAME: **Indrajit Srivastava**

eRA COMMONS USER NAME (credential, e.g., agency login): **INDRAJIT_SRIVASTAVA**

POSITION TITLE: **Assistant Professor in Mechanical Engineering**

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YY	FIELD OF STUDY
Indian Institute of Engineering Science and Technology, Shibpur, WB, India	B.S.	05/15	Metallurgical Engineering & Materials Science
University of Illinois at Urbana-Champaign, IL	M.S.	05/17	Bioengineering
University of Illinois at Urbana-Champaign, IL	Ph.D.	05/20	Bioengineering
University of Illinois at Urbana-Champaign, IL	Post-Doc	05/23	Cancer Nanotechnology

A. Personal Statement

My research is focused on leveraging the unique biomimetic characteristics of natural materials (membranes, proteins, exosomes, etc.) and using nanoengineering design principles to make nanoparticles for early detection, diagnosis/prognosis, and image-guided interventions for diseases like cancer, cardiovascular diseases, kidney diseases, and bacterial and viral pathogenesis. My past academic training and research experiences have provided me with an excellent background in multiple disciplines including materials science, chemistry, and bioengineering which allows me to uniquely approach any given problem. I have extensive and expansive training in cancer research that began as an undergraduate researcher and continued to my graduate degree and postdoctoral work. As an undergraduate researcher in Dr. Dipanjan Pan's laboratory at Mills Breast Cancer Institute, I developed novel polymeric nanoparticles made from "*hyperstar*" polymers, that could encompass multiple FDA-approved drugs targeting triple-negative breast cancer with high specificity and selectivity in *in vitro* and *in vivo* tumor models. For my doctoral studies in Dr. Dipanjan Pan's laboratory at Mills Breast Cancer Institute and Department of Bioengineering at the University of Illinois at Urbana-Champaign (UIUC), I investigated how size, surface charge, and surface functionality influence the (i) fluorescent properties of carbon-based nanoparticles (called "*Carbon Dots*" or *CDots*) and (ii) impacts their endocytosis in cancer cells of varying pathophysiology. These facilitated a better understanding of nanoparticle-biological interactions and integrating this knowledge with pathophysiology allowed us to engineer nanomedicines with a superior likelihood of crossing the endocytic "barrier" for drug delivery, multi-scale bioimaging, and biosensing [a, b]. During my postdoctoral training in the labs of Drs. Shuming Nie and Viktor Gruev at the Cancer Center of Illinois, UIUC, I was at the forefront of development of a new class of surface-enhanced Raman scattering (SERS) nanosensors that is significantly brighter than current SERS nanosensors in literature, has dramatic improvements in stability and dispersibility, and could be easily imparted with tumor-targeting features to be used for *in vitro* diagnostics, and spectroscopy-guided cancer surgery. [c] I further spearheaded the development of ratiometric cell membrane-coated near-infrared fluorescent organic dye encapsulated nanoparticles for image-guided surgery of lung metastases in *in vivo* mouse models and *ex vivo* tumor-mimicking phantoms. [d] During my postdoctoral training, I assisted Dr. Viktor Gruev's laboratory during clinical trials that involved data collection and analysis of human patient tumor samples using several bioinspired camera sensors [e]. This opportunity allowed me to interact

closely with clinicians, surgeons, and engineers from Washington University at St. Louis and the University of Pennsylvania, thus expanding my network.

Recent publications relevant for cancer research: The following papers highlights my extensive academic training and experiences in conducting cancer research that spanned from developing optical imaging and spectroscopic probes for tumor detections and assisting in translating new camera imaging technologies towards clinical trials.

(§ denotes corresponding author, * denotes co-first author)

a. H. Nguyen,* I. Srivastava,* D. Pan,§ M. Gruebele,§ "Unraveling the Fluorescence Mechanism of Carbon Dots with Sub-Single-Particle Resolution". ACS Nano 2020, 14, 5, 6127-6137. PMID: 32324372.

b. I. Srivastava, P. Moitra, M. Fayyaz, S. Pandit, T. L. Kampert, P. Fathi, H. R. Alanagh, K. Dighe, M. Alafeef, K. Vuong, M. Jabeen, S. Nie, J. Irudayaraj, D. Pan,§ "Rational Design of Surface-State Controlled Multicolor Cross-Linked Carbon Dots with Distinct Photoluminescence and Cellular Uptake Properties." ACS Applied Materials & Interfaces 2021, 13 (50), 59747-59760. PMID: 34878252.

c. I. Srivastava, R. Xue, J. Jones, H. Rhee, K. Flatt, V. Gruev,§ S. Nie,§ "Biomimetic Surface-Enhanced Raman Scattering Nanoparticles with Improved Dispersibility, Signal Brightness, and Tumor Targeting Functions." ACS Nano 2022, 16, 5, 8051-8063. PMID: 35471820

d. I. Srivastava,§ B. Lew, Y. Wang, S. Blair, M. B. George, B. S. Hajek, S. Bangru, S. Pandit, Z. Wang, J. Ludwig, K. Flatt, M. Gruebele, S. Nie,§ V. Gruev,§ "Cell-Membrane Coated Nanoparticles for Tumor Delineation and Qualitative Estimation of Cancer Biomarkers at Single Wavelength Excitation in Murine and Phantom Models." ACS Nano 2023, 17, 9, 8465-8482. PMID: 37126072.

e. C. Chen, Z. Wang, J. Wu, Z. Deng, T. Zhang, Z. Zhu, Y. Jin, B. Lew, I. Srivastava, Z. Liang, S. Nie,§ V. Gruev,§ "Bioinspired, Vertically Stacked, and Perovskite-Nanocrystal Enhanced CMOS Imaging Sensors for Resolving UV Spectral Signatures in Cancer Cells." *Sci. Adv.* 9, eadk3860, 2023.

B. Positions and Honors

Positions and Employment

07/2020-05/2023	Postdoctoral Research Associate, Departments of Bioengineering and Electrical & Computer Engineering, University of Illinois at Urbana-Champaign, Urbana, IL
01/2020-05/2023	Graduate Teaching Assistant, Department of Bioengineering, University of Illinois at Urbana-Champaign, Urbana, IL
08/2018-012/2018	Graduate Teaching Assistant, Department of Bioengineering, University of Illinois at Urbana-Champaign, Urbana, IL
08/2015-12/2019	Graduate Research Assistant, Department of Bioengineering, University of Illinois at Urbana-Champaign, Urbana, IL
05/2014-07/2014	Summer Undergraduate Researcher, Mills Breast Cancer Institute, Carle Foundation Hospital, Urbana, IL

Honors

2023	Postdoctoral Scholars Recognition Program Recipient: Leadership in Mentoring, American Chemical Society
2023	CAS Future Leaders Top 100 Program, American Chemical Society
2023	Selected Participant for ACS New Faculty Workshop, American Chemical Society
2022	Baxter Young Investigator Award, Baxter International Foundation
2022	Postdoc to Faculty (P2F) Scholar Award, American Chemical Society
2022	Younger Chemists Committee Leadership Development Award, American Chemical Society
2021	Baxter Young Investigator Award, Baxter International Foundation
2021	BMES UNITE Future Faculty Fellow, Biomedical Engineering Society

2021 Extended Advisory Board Member, Carbon Journal Elsevier
2021 Outstanding Thesis in Carbon Science & Technology, 2nd place, Carbon Journal Elsevier
2021 PMSE Future Faculty Scholar, American Chemical Society
2021 Alexander von Humboldt Research Fellowship, Alexander von Humboldt
2020 Biomedical Engineering Society (BMES) Career Development Award
2020 Graduate College Travel Fellowship Award, UIUC
2020 Biomedical Engineering Society (BMES) Midwest Graduate Speaker Exchange Award
2019 Outstanding Mentorship Award, WYSE Research Programs, UIUC
2019 Bioengineering Teaching Excellence Fellowship Award, UIUC
2018 Graduate College Travel Fellowship Award, UIUC
2013-2014 Prof. A. K. Seal Undergraduate Academic Fellowship
2012 Second Place in Poster Competition, *'Metallum'* by IIEST Shibpur
2009 Silver Medal, National Mathematics Olympiad, All India Mathematics Teachers Association
2008 Bronze Medal, National Science Exhibition, Central Board of Secondary Education

Professional Membership

2022- Member, American Heart Association American Chemical Society
2020- Member, Biomedical Engineering Society
2018- Member, American Chemical Society

C. Contributions to Science

1. My early research contribution to the field of cancer research

As an undergraduate researcher, I focused on applying my burgeoning knowledge of materials science and chemistry courses to synthesize, optimize, and characterize novel polymeric nanoparticle-based carriers constituting of *"hyperstar"* polymers. These polymeric nanocarriers were used for combinatorial therapy due its ability to encompass multiple FDA-approved drugs that selectively targeted triple-negative breast cancer cell proliferation *via* STAT3 and topoisomerase-II pathways [a]. The so called "*nanococktail*" demonstrated 4-fold proficiency than individual drugs and ~20 times more selective than the parent drugs in *in vitro* and *in vivo* studies.

a. S. K. Misra, X. Wang, I. Srivastava, M. K. Imgruet, R. W. Graff, A. Ohoka, T. L. Kampert, H. Gao, § D. Pan,§ "Combinatorial Therapy for Triple Negative Breast Cancer Using Hyperstar Polymer-Based Nanoparticles." Chem. Comm. 2015, 51, 16710. PMID: 26434941.

2. Synthesis and development of carbon dots with high quantum yield and multi-color emission

I elucidated an in-depth understanding of the fluorescence mechanisms of carbon dots (CDots) both at ensemble (bulk) state as well as single-particle level, revealing that fluorescence emission in CDots are correlated with abundance of oxygen-rich groups (hydroxyl, carboxyl) at their nanoscale surface [a]. I collaborated with Dr. Martin Gruebele and using their in-house scanning tunneling microscopy setup, directly imaged individual CDots with sub-particle resolution and observed that their emission spectra to be correlated with their surface defects [b]. Additionally, I utilized a combination of X-ray photoelectron spectroscopy (XPS), Fourier-transform infrared spectroscopy (FTIR) and pH-dependent fluorescence titrations to confirm the surface defects on CDots were composed of oxygen-rich groups. Leveraging these findings, I established new methods for chemical synthesis in fabricating multi-color emitting CDs with high quantum yields [c] and used them for multiscale imaging of tumor cells [d]. I also established new methods for preparing "*switchable*" CDs i.e., ability of CDs to switch off-switch on their fluorescence in presence of an external trigger (like macromolecular coating, tumor hypoxia, or ultraviolet light) [e, f].

a. I. Srivastava, J. S. Khamo, S. Pandit, P. Fathi, X. Huang, A. Cao, R. Haasch, S. Nie, K. Zhang, D. Pan, § "Influence of electron acceptor and electron donor on the photophysical properties of carbon dots: a comparative investigation at the bulk-state and single-particle level." *Adv. Funct. Mater.* 2019, 29, 1902466.
b. H. Nguyen,* I. Srivastava,* D. Pan,§ M. Gruebele,§ "Unraveling the fluorescence mechanism of carbon dots with sub-single-particle resolution." *ACS Nano*, 2020, 14, 6127. PMID: 32324372.

c. I. Srivastava, S. K. Misra, I. Tripathi, A. S. Schwartz-Duval, D. Pan,§ "In situ time-dependent and progressive oxidation of reduced state surface functionalities at the nanoscale of carbon nanoparticles for polarity driven multi-scale near-infrared imaging." *Adv. Biosys.* 2018, 2, 1800009.

d. I. Srivastava, P. Moitra, M. Fayyaz, S. Pandit, T. L. Kampert, P. Fathi, H. R. Alanagh, K. Dighe, M. Alafeef, K. Vuong, M. Jabeen, S. Nie, J. Irudayaraj, D. Pan,§ "Rational Design of Surface-State Controlled Multicolor Cross-Linked Carbon Dots with Distinct Photoluminescence and Cellular Uptake Properties." ACS Appl. Mater. Interfaces 2021, 13 (50), 59747-59760. PMID: 34878252.

e. S. K. Misra,* I. Srivastava,* I. Tripathi, E. A. Daza, F. Ostadhossein, D. Pan,§ "Macromolecularly "caged" carbon nanoparticles for intracellular trafficking via switchable photoluminescence." *J. Am. Chem. Soc.* 2017, 139, 1746. PMID: 28016386.

f. I. Srivastava, S. Bangru, K. Brent, E. Altun, S. Pandit, A. Kalsotra, D. Pan.§ "Biodegradable and switchable near-infrared fluorescent probes for detection of hypoxia." PMID: 37610080.

3. Interaction of carbon dots with biological entities

I investigated how CDots interacted with several biological entities including enzymes, proteins, and cancer cells. I studied the metabolic fate and biodegradation patterns of CDots having varying surface chemistries in presence of human digestive enzymes such as lipase and myeloperoxidase [a]. I extensively investigated the protein corona formation on CDots in presence of human plasma by with tuning their size and surface chemistries using an on-chip electrical monitoring platform [b]. Such a platform when combined with time series analysis and statistical tools allowed the visualization of the "soft" corona and "hard" corona components on nanoparticles for the first time under a fluidic condition analogous to blood flow. I further studied how surface chemistry of CDots influences the polymerization activity of a tubulin converting into microtubules, (vital for cellular processes). This information can be leveraged into using CDots as a natural therapeutic target for cancer [c]. Using flow cytometry and confocal microscopy, I explored how the interplay of size and surface chemistry of CDots influences their cellular internalization in breast cancer cells of varying stages based on their pathophysiology [d]. Additionality, I designed pH-responsive oligonucleotide decorated CDots and utilized them to deliver intracellular cargo and monitor biological events, including apoptosis and intracellular Ca^{2+} ion concentration [e].

a. I. Srivastava,* D. Sar,* P. Mukherjee, A. S. Schwartz-Duval, Z. Huang, C. Jaramillo, A. Civantos, I. Tripathi, J. P. Allain, R. Bhargava, D. Pan, "Enzyme-catalyzed biodegradation of carbon dots follows sequential oxidation in a time dependent manner." *Nanoscale*, 2019, 11, 8226. PMID: 30973556.

b. I. Srivastava, M. S. Khan, K. Dighe, M. Alafeef, Z. Wang, T. Banerjee, T. Ghonge, L. Grove, R. Bashir, D. Pan, "On-chip electrical monitoring of real-time "soft" and "hard" protein corona formation on carbon nanoparticles." *Small Methods*, doi: 10.1002/smtd.202000099.

c. P. Mukherjee,* I. Srivastava,* A. Ghosh, H. Jang, J. Pfister, D. Pan*,R. Bhargava.* "Real-time Chemical Imaging of Carbon Dot Templated Tubulin-Polymerization". Submitted.

d. I. Srivastava,* S. K. Misra,* F. Ostadhossein, E. Daza, J. Singh, D. Pan, "Surface chemistry of carbon nanoparticles functionally select their uptake in various stages of cancer cells." *Nano Research* 2017, 10, 3269.

e. I. Srivastava,* S. K. Misra,* S. Bangru, K. A. Boateng, J. A. N. T. Soares, A. S. Schwartz-Duval, A. Kalsotra, D. Pan, "Complementary oligonucleotide conjugated multicolor carbon dots for intracellular recognition of biological events." *ACS Appl. Mater. Interfaces* 2020, 12, 16137. PMID: 32182420.

4. Cell-membrane coated nanosensors for early-disease diagnostics and image-guided surgical interventions

While in Dr. I pioneered the design and development of a new class of cell-membrane-coated SERS plasmonic nanoparticles/nanotags [a]. Under similar experimental conditions, these nanoparticles were significantly brighter in their SERS signal profile (~5x) when compared to the PEGylated SERS nanoparticles/nanotags [Nie, S. et al., *Nat. Biotechnol* 2008], one of the brightest SERS nanotags reported in literature. I further demonstrated that these biomimetic SERS nanoparticles had enhanced dispersion stability features, including resistance to freeze-thaw cycles, heating, and physiological solutions, and could be easily lyophilized into powders. I integrated tumor-targetability features to these nanoparticles and demonstrated their ability in *in vitro* spectroscopic detection of metastatic tumor cells (detecting as low as ~1000 tumor cells) and for multi-modal image-guided resections of tumor cell-mimicking phantoms (SERS + photoacoustic). [b] In parallel, I led the development of ratiometric near-infrared fluorescent nanoparticle pairs with a cell-membrane coating and targeted two distinct cancer cell-surface biomarkers. These cell-membrane coated fluorescent probes demonstrated favorable *in vivo* biological properties compared to conventional nanoparticle agents (improved biocompatibility, prolonged blood

circulations, reduced Kupffer cell uptake) and superior optical properties (specific fluorescence enhancement in tumor regions with high tumor-to-normal tissue ratios (~9), significantly higher than the clinically defined Rose criterion. These ratiometric nanoparticles targeted two different cancer cell-surface biomarkers (folate, αvβ3) while having distinct emissions (720nm, and 840nm, respectively) allowing us to estimate cancer cell-surface biomarkers distribution in solid tumors at single wavelength excitation, providing insights into cancer progression such as metastases.

a. I. Srivastava, R. Xue, J. Jones, H. Rhee, K. Flatt, V. Gruev, S. Nie, "Biomimetic Surface-Enhanced Raman Scattering (SERS) Nanoparticles with Improved Dispersibility, Signal Brightness, and Tumor Targeting Functions". ACS Nano 2022, 16, 5, 8051-8053. PMID: 35471820

b. I. Srivastava,§ B. Lew, Y. Wang, S. Blair, M. B. George, B. S. Hajek, S. Bangru, S. Pandit, Z. Wang, J. Ludwig, K. Flatt, M. Gruebele, S. Nie,§ V. Gruev,§ "Cell-Membrane Coated Nanoparticles for Tumor Delineation and Qualitative Estimation of Cancer Biomarkers at Single Wavelength Excitation in Murine and Phantom Models." ACS Nano 2023, 17, 9, 8465-8482. PMID: 37126072.

c. R. Xue, H.-K. Huang, Z. Wang, J. Jones, I. Vasquez, I. Garza, K. Hayes, K. Galinsky, S. Pandit, L. Lin, S. Zhao, K. Flatt, V. Gruev, I. Srivastava,§ Y.-S. Chen,§ S. Nie,§ "Biomimetic Membrane Protected Plasmonic Nanostructures as Dual-Modality Contrast Agents for Correlated SERS and Photoacoustic Detection of Hidden Tumor Lesions". *ACS Appl. Mater. Interfaces, Minor revision*.

Completed List of Published Work on PubMed:
https://pubmed.ncbi.nlm.nih.gov/?term=srivastava+indrajit

- 32 total peer-reviewed publications, 15 publications as first/co-first author, or co-senior author
- >1100 citations, h-index = 19, determined using Google Scholar on October 4, 2023