BIOGRAPHICAL SKETCH

NAME: Kedar Narayan

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

POSITION TITLE: Group Leader and Senior Scientist, CCR volume electron microscopy, Frederick National Laboratory, National Cancer Institute

EDUCATION/TRAINING

DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
BSc	06/2000	Chemistry
Diploma	08/2000	Software engineering
MA	06/2002	Pathology
PhD	06/2009	Immunology
Post-doc	10/2014	Electron microscopy
	(if applicable) BSc Diploma MA PhD	(if applicable)Date MM/YYYYBSc06/2000Diploma08/2000MA06/2002PhD06/2009

A. Personal Statement

My vision is to establish volume electron microscopy (vEM) as a quantitative analytical approach in biological and clinical research. The central idea inspiring my work is that by combining efficient, high-resolution 2D and 3D imaging of cells and tissue ultrastructure with cutting-edge AI and computational tools, I can create new parameters of measurement of states and fates in cancer and in cell biology in general.

I am currently Group Leader at CCR volume electron microscopy (CvEM) at Frederick National Laboratory and National Cancer Institute. I successfully built an integrated volume EM laboratory from the ground up, and I continue to develop new vEM and correlative techniques and deploy them in collaboration with NIH scientists to answer important questions in various biological systems. My wide-ranging education and experience mean that I am at ease with all "five pillars" of our work: i. *artifact-free sample preparation* ii. *efficient vEM imaging* iii. *registration and correlation strategies* iv. *segmentation and analysis pipelines*, and v. *data handling and standards*. I partner with outside technology and subject matter experts to add to my own strengths and produce technical advances and biological insights. Crucially, I have incorporated cutting-edge AI approaches to mitigate data analysis bottlenecks in vEM, exemplified by our open source napari plugin *empanada* for 3D organelle segmentation which is widely used by the vEM community. We have also created solutions to handle large data and to generate appropriate metadata for FAIR sharing. Together, my work has resulted in high-impact and well cited publications as well as several invention reports and awards.

In parallel with my research, I play a leading role creating a world-wide vEM community to bring these approaches into the mainstream. I am committed to the hard work of bridging the gaps between tech-savvy/well-funded groups and smaller labs/core facilities. I have mentored underrepresented high-school, undergraduate, and graduate students; several have won local and state level prizes for their work. Overall, I have in addition to vEM expertise, the ability to both "think large" about the science as well as zoom in to specific experimental minutiae; the experience of building a highly collaborative group from scratch; and the motivation to develop and apply a nascent technology within a resilient framework to transform biology.

B. Positions, Scientific Appointments, and Honors (community work listed in section C)

2000 2000 - 2002 2002 - 2004	Best Outgoing Student, Department of Chemistry, Loyola College Rajiv Gandhi Scholarship (full tuition and stipend), University of Cambridge Graduate Student Fellowship (full tuition and stipend), Johns Hopkins
2005 2005, 2006	Graduate Research 1st place, Society for Experimental Biology, DC chapter Young Investigator Award, Department of Pathology, Johns Hopkins
2000, 2000	Graduate Student Travel Award, Johns Hopkins
2007	Young Scientist Award, Association for Scientists of Indian Origin in America
2009	Visiting Fellow, National Cancer Institute (NCI), NIH
2010, 2012	Fellows Award for Research Excellence, NIH
2011	Research Fellow, NIH
2015	Scientist II, Frederick National Laboratory (FNL), NCI
2018, 2020	LDER grant awardee, FNL
2019	Group Leader and Sr Scientist, FNL, NCI
2019	Nominee, Mentor of the Year, NCI
2020	Member, EMBL/EBI imaging ecosystem working group
2021	Member, EMBL core facilities advisory panel
2021	Member, NIH.AI steering committee
2023	Director's Innovation Award, Cancer Research Tech Program, FNL
2023	Director's Award for Data Science, NCI
2023, 2024	Technology Transfer Award, NCI
2024	Technical Publication Award, FNL (Leidos)
2025	Alan Agar Award, Royal Microscopy Society

Funding

My work is funded through federal funds from the National Cancer Institute, National Institutes of Health, under Contract No. 75N91019D00024. Extra funding/awards listed below:

2017-2019 CRADA funding from Zeiss Inc. to develop cryo-correlative imaging tissues.

2018-2020 LDER funding from FNL for characterization of anaphase catastrophe in cancer cells.

2023 Director's Grant, FNL to create data models for volume EM

2024-2025 Discovery Development Program funding to develop analysis pipelines in volume EM

C. Contributions to Science

a. Studies of virus-cell interactions in 3D

My post-doctoral work at NIH focused on adapting FIB-SEM technology, then used primarily in materials sciences, to biology, specifically to image HIV-cell interactions. I led these efforts within the group, leading to co-first authored papers describing the HIV virological synapse between dendritic cells and T cells, as well as between uninfected and infected CD4+ T cells. I also used the FIB as a preparatory tool for chemical imaging and cryo EM workflows, and the "chevron pattern"-based loop to control FIB progression in resinembedded specimens (developed in collaboration with industrial partners) is now standard in commercial acquisition software. During the COVID pandemic, my group applied FIB-SEM to SARS-CoV-2 infected cells *in vitro* to reveal effects of membrane curvature and tight junctions on viral budding.

[1] Felts, R.L.*, Narayan, K.*, et al., 3D visualization of HIV transfer at the virological synapse between dendritic cells and T cells. PNAS, 2010.

[2] Narayan, K. and S. Subramaniam, Focused ion beams in biology. Nat Methods, 2015.

[3] Baena, V., et al., FIB-SEM as a Volume Electron Microscopy Approach to Study Cellular Architectures in SARS-CoV-2 and Other Viral Infections: A Practical Primer for a Virologist. Viruses, 2021.

b. Applications of correlative volume EM in cancer and cell biology

After establishing my group at Frederick National Laboratory, I focused on broadening the applications of volume EM in cell biology, particularly if multiple approaches could be used in combination or correlated with light microscopy. In various collaborations, my group used correlative vEM to characterize important cellular features such as mitochondrial networks, structural intermediates in ciliogenesis and nuclear envelope breakdown in various experimental systems including *C. elegans* and *D. melanogaster*. With an exploratory

research grant, we characterized anaphase catastrophe induced in cancer cells by a drug candidate. To enable the interrogation by vEM of systems that require fine temporal control, we developed a CRADA-funded workflow to image transient intermediates in thick samples, trapped by high-pressure freezing, imaged by cryo-fluorescence microscopy and then by correlative room temperature vEM imaging.

[4] Rahman, M., et al., *C. elegans pronuclei fuse after fertilization through a novel membrane structure.* J Cell Biol, 2020.

[5] Kang, S. W. S., et al., A spatial map of hepatic mitochondria uncovers functional heterogeneity shaped by *nutrient-sensing signaling*. Nat Commun, 2024.

[6] Tyutyunyk-Massey, L., et al., CDK2 Inhibition Produces a Persistent Population of Polyploid Cancer Cells. JCI Insight, 2025.

c. Deep Learning based methods in vEM

A known bottleneck in the vEM experimental pipeline is the segmentation of features of interest from these massive 3D datasets; we are addressing this by developing cutting-edge AI based approaches. We recently released a curated 1.5 x 10⁶ image unlabeled training dataset of relevant, heterogenous, information-rich and non-redundant cellular EM images, as well as a corresponding dataset of ~135,000 labeled mitochondria, both the largest of their kind. *MitoNet*, a generalist deep learning model trained on these resources, reports state-of-the-art segmentation results on diverse mitochondria. We also released *empanada*, an easy-to-use napari plugin to allow biologists to facilely segment features of interest using these models and correct errors in model predictions. *empanada* has been downloaded > 4000 times, suggesting deep penetration and use by the vEM community, and we continue to develop more powerful AI tools, with the ultimate target of push-button segmentation of any organelle from any vEM dataset.

[7] Conrad, R. and Narayan, K. CEM500K, a large-scale heterogeneous unlabeled cellular electron microscopy image dataset for deep learning. eLife, 2021.

[8] Conrad, R. and Narayan, K. Instance segmentation of mitochondria in electron microscopy images with a generalist deep learning model trained on a diverse dataset. Cell Syst 2023.

d. Standards and community work

I play an active role in positively shaping the nascent vEM community. I co-organized the first "large data" symposia at Microscopy & Microanalysis, and a virtual vEM conference in 2020 to define the obstacles and "wish lists" in the field. I am on the Scientific Advisory Boards of the CZI funded volume EM community initiative and EuroBioImaging, and I co-chair the vEM community data working group. I have. I have worked with European Bioinformatics Institute (EBI) to articulate vEM and CLEM metadata standards recommendations and create a structured widget to standardize and share EM sample preparation protocols. I am on a committee for standardization at Frederick National Laboratory, and on NIH's advisory panel on artificial intelligence. I co-edited a methods book on volume EM and co-authored an authoritative vEM methods primer with leaders in the vEM field. My aim is to articulate volume EM as a scientific field and to identify (and work collaboratively to remove) obstacles to add vEM to the imaging toolkit for any cell biologist and clinical researcher.

[9] Sarkans, U., et al., *REMBI: Recommended Metadata for Biological Images-enabling reuse of microscopy data in biology.* Nat Methods, 2021.

- [10] Peddie, C. L., et al., Volume electron microscopy. Nat Rev Methods Primers, 2022
- [11] Bajcsy, P., et al., Enabling global image data sharing in the life sciences. Nat Methods, 2025

Community contributions

2014 -	Member, Microscopy Society of America
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- 2018 2022 Secretary, Chesapeake Microscopy & Microanalysis Society
- 2018 Mentor, Warner H Kirsten Student Internship program, National Cancer Institute
- 2019, 2021 Co-organizer, Microscopy & Microanalysis symposium: large data in cell biological imaging 2020 Organizer, microlab/symposium on volume EM
- 2020 Co-chair, volume EM Data working group, UK vEM initiative
- 2020 Standards, References and Training Executive Committee, Frederick National Laboratory
- 2022 Scientific Advisory Board, EuroBioImaging
- 2023 Scientific Advisory Board, CZI volume EM community tools
- 2023 Vice Chair, Gordon Research Conference on volume EM
- 2023 Organizer, Microscopy & Microanalysis: volume EM symposium

2023	Organizer, volume EM Standards Conference
2024	Organizer, "Volume EM 101" workshop
2024 -	Mentor, Frederick County Public School Work Based Learning Program
2025	Chair, Gordon Research Conference on volume EM

Full bibliography

https://www.ncbi.nlm.nih.gov/myncbi/kedar.narayan.1/bibliography/public/

Media (available outside FNL, NCI)

Focal plane (Alan Agar Award interview) https://focalplane.biologists.com/2024/12/14/volumeem-an-interview-with-kedar-narayan/

The microscopists (podcast, interview) https://www.youtube.com/watch?v=Lx-h0LZtENY

Volume EM: Concepts, Correlations & Computations https://www.youtube.com/watch?v=w4qXFvUekIg

Introduction to focused ion beam scanning electron microscopy (FIB-SEM) <u>https://www.youtube.com/watch?v=zqW6pXaU4Go</u>

Data set lets AI teach itself to analyze microscopy better <u>https://frederick.cancer.gov/node/645</u>

Newly published metadata standards for biological imaging aim to make data sets more accessible https://frederick.cancer.gov/news/newly-published-metadata-standards-biological-imaging-aim-make-data-sets

'Empanada' is a leap forward in rapid 3-D image processing and annotation <u>https://frederick.cancer.gov/news/empanada-leap-forward-rapid-3-d-image-processing-and-annotation</u>