BIOGRAPHICAL SKETCH

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NAME: Kapitonova, Mariia

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

POSITION TITLE: Chemistry Graduate Research Assistant

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE MM/YYYY	COMPLETION DATE MM/YYYY	FIELD OF STUDY
Lomonosov Moscow State University, Moscow	MS	09/2014	09/2020	Fundamental and Applied Chemistry
University of Delaware, Newark, DE	PHD	09/2021	09/2026	Chemistry and Biochemistry
Institute of Protein Research, Pushchino, Moscow District	Other training	06/2018	07/2018	Summer School in Molecular Biology

A. Personal Statement

As a fourth-year Ph.D. candidate in Professor Rozovsky's research group, I have gained extensive experience and numerous opportunities to develop my skills in research, scientific communication, and mentoring. Most importantly, I have cultivated a deep passion for using science—particularly molecular biology and biochemistry—to address global challenges. In Professor Rozovsky's lab, we study the structure of selenoproteins—proteins that contain selenium—with the goal of uncovering insights that could contribute to drug development and novel therapies. Since selenoproteins play key roles in multiple stress response pathways in the body, understanding their structure and function has significant biomedical implications. Looking ahead, I envision myself in five years combining my passion for protein structure and protein design with another critical interest—developing solutions to the climate crisis. These two fields have recently converged with the discovery and engineering of proteins capable of breaking down commonly used plastics. To prepare for research in this area, I have deepened my expertise in structural biology as part of Professor Rozovsky's team and broadened my understanding of climate-related challenges through my involvement in the Graduate Student Organization Climate Fellows program.

B. Positions and Honors

Positions and Scientific Appointments

2021 - Chemistry Graduate Research Assistant, University of Delaware, Chemistry and Biochemistry Department, Newark, DE

2021 - 2021 Scientific Analyst, Innovation center "Biruch" of the fat and-oil company "EFCO", Moscow

2021 - 2021 Transcriber and Editor of Digital Chemistry Lectures, Lomonosov Moscow State University, Moscow

2016 - 2022 Undergraduate Research Assistant, A.N. Belozersky Institute Of Physico-Chemical Biology MSU, Department of nucleic acids chemistry / Institute of Gene Biology (IGB) of the Russian Academy of Sciences, Moscow

2015 - 2018 Undergraduate Research Assistant, Lomonosov Moscow State University, Department of Chemistry, Organic Chemistry Subdepartment , Moscow

Honors

2025 Glenn S. Skinner Award for Excellence in Scholarship, Teaching and Research, University of Delaware, Chemistry and Biochemistry Department

2024 Short-talk speaker selection, 2024 Frontiers in Chemistry and Biology Interface Symposium

2020	State Academic Scholarship for Success in Research Activities , Lomonosov Moscow State University
2019	Diploma for the best oral presentation, International Conference for Students and Young Scientists "Lomonosov"
2015	Diploma for the best oral presentation, International Conference for Students and Young Scientists "Lomonosov"

C. Contribution to Science

1. SYNTHESIS OF 2,2'-BIPYRIDYL-BASED EUROPIUM COMPLEX AND INVESTIGATION OF ITS INTERACTION WITH HUMAN SERUM ALBUMIN BY IR SPECTROSCOPY, FLUORIMETRY AND SPECTROPHOTOMETRY
   a. Kharcheva A, Kapitonova M, Farat O, Borisova N, Patsaeva S. The interaction of the europium complex with human serum albumin. International Symposium on Optics and Biophotonics VI: Saratov Fall Meeting 2018; 2018 September 24; Saratov, Russian Federation. https://www.spiedigitallibrary.org/conference-proceedings-of-spie/11065/2523257/The-interaction-of-the-europium-complex-with-human-serum-albumin/10.1117/12.2523257.short?SSO=1&tab=ArticleLink: SPIE; c2019. Available from: https://doi.org/10.1117/12.2523257 DOI: 10.1117/12.2523257
2. RESEARCH OF THE CELLULAR PROTEIN KU70 ROLE IN HIV-1 REPLICATION
   a. Kapitonova MA, Shadrina OA, Korolev SP, Gottikh MB. [Main Approaches to Controlled Protein Degradation in the Cell]. Mol Biol (Mosk). 2021 Jul-Aug;55(4):543-561. PubMed PMID: 34432773.
3. Structural and functional studies of selenoprotein S and selenoprotein K
   a. Odunsi A, Kapitonova MA, Woodward G, Rahmani E, Ghelichkhani F, Liu J, Rozovsky S. Selenoprotein K at the intersection of cellular pathways. Arch Biochem Biophys. 2025 Feb;764:110221. PubMed Central PMCID: PMC11750610.
   b. Ghelichkhani F, Gonzalez FA, Kapitonova MA, Rozovsky S. Selenoprotein S Interacts with the Replication and Transcription Complex of SARS-CoV-2 by Binding nsp7. J Mol Biol. 2023 Apr 15;435(8):168008. PubMed Central PMCID: PMC9911985.
   c. Ghelichkhani F, Gonzalez FA, Kapitonova MA, Schaefer-Ramadan S, Liu J, Cheng R, Rozovsky S. Selenoprotein S: A versatile disordered protein. Arch Biochem Biophys. 2022 Nov 30;731:109427. PubMed Central PMCID: PMC10026367.

D. Scholastic Performance

Scholastic Performance

YEAR	COURSE TITLE	GRADE
	LOMONOSOV MOSCOW STATE UNIVERSITY	
2014	History	Passed
2014	Computer Sciences	Passed
2014	Mathematical Analysis	Passed
2014	Laboratory Practicum in Inorganic Chemistry	Passed
2014	Chemical Biology and Introduction to Cell Biology	Passed
2014	English language	Passed
2014	Inorganic Chemistry	Good
2014	Mathematical Analysis	Excellent
2014	Analytical Geometry	Passed
2014	Physical Training	Passed
2015	Elective Courses in Physical Education	Passed
2015	English Language	Passed
2015	Mathematical Analysis	Good
2015	Laboratory Practicum in Inorganic Chemistry	Passed
2015	Linear Algebra	Passed

2015	Computer Sciences	Excellent
2015	Inorganic Chemistry	Good
2015	Mechanics. Electricity	Good
2015	Chemical Biology and Introduction to Cell Biology	Excellent
2015	Course Paper in Inorganic Chemistry	Excellent
2015	Analytical and Preparative Biochemistry	Passed
2015	Analytical Chemistry	Passed
2015	Laboratory Practicum in Analytical Chemistry	Passed
2015	Elective Courses in Physical Education	Passed
2015	English Language	Passed
2015	Probability Theory	Good
2015	Mathematical Analysis	Excellent
2015	Laboratory Practicum in Physics	Passed
2015	Oscillations and Waves. Optics	Good
2016	Life safety	Passed
2016	History of the Faculty of Chemistry	Passed
2016	Equations of Mathematical Physics	Passed
2016	Elective Courses in Physical Education	Passed
2016	Theoretical Mathematics	Passed
2016	Russian Language and Standard of Speech	Passed
2016	Laboratory Practicum in Analytical Chemistry	Passed
2016	Mathematical Analysis	Excellent
2016	Analytical Chemistry	Excellent
2016	Elements of Applied Mathematical Statistics	Excellent
2016	English Language	Excellent
2016	Course paper in Bioanalytical Chemistry	Excellent
2016	Laboratory Practicum in Organic Chemistry	Passed
2016	Introduction to Physics of Nanostructures	Passed
2016	Economics	Passed
2016	Molecules and Diseases	Passed
2016	Organic Chemistry	Excellent
2016	Modern Natural Sciences	Passed
2016	Principles of Physiology and Immunology	Passed
2016	Foundations of Quantum Mechanics	Good
2016	Fundamentals of Radiochemistry and Radioecology	Good
2017	Bioinformatics for Next-Generation Sequencing	Passed
2017	Elements of the Structure of Matter	Passed
2017	Bioorganic Chemistry	Passed
2017	Laboratory Practicum in Organic Chemistry	Passed
2017	Organic Chemistry	Excellent
2017	History	Excellent
2017	Quantum Chemistry and Molecular Structure	Excellent
2017	Chemical Foundations of Biological Processes	Excellent
2017	Economics	Excellent
2017	Course Paper in Organic Chemistry	Excellent
2017	Laboratory Practicum in Colloidal Chemistry	Passed
2017	Laboratory Practicum in Physical Chemistry	Passed
2017	Introduction to Mathematical and Computer Modeling of Bio- and Nanostructures	Passed
2017	Fundamentals of Biochemistry	Passed

2017	Modern Ecologic problems and sustainable development	Passed
2017	Physical Chemistry	Excellent
2017	Colloidal Chemistry	Good
2017	Protein Chemistry	Excellent
2017	Introduction to Specialty “Bioorganic Chemistry”	Passed
2017	Jurisprudence	Excellent
2018	Polymers	Passed
2018	Research Work	Passed
2018	Philosophy	Passed
2018	Biophysics in Practical Medicine	Passed
2018	Nanobiomaterials and Physics of Nanostructures	Excellent
2018	Crystal Chemistry	Passed
2018	Laboratory Practicum in Physical Chemistry	Passed
2018	Physical Chemistry	Good
2018	Course Paper in Physical Chemistry	Excellent
2018	Research Work	Passed
2018	Advanced Practical Course in Bioorganic Chemistry	Passed
2018	Personality and Culture	Passed
2018	Methods for Study of Proteins and Nucleic Acids	Passed
2018	Molecular Biology of the Gene	Passed
2018	Philosophy	Excellent
2018	History and Methodology of Chemistry	Excellent
2018	Methods of Physical Biochemistry	Good
2018	Laboratory Practicum in Polymers	Passed
2018	Polymers	Excellent
2018	Chemistry of Nucleic Acids	Good
2019	Research Work	Passed
2019	Methods of Molecular Biology	Good
2019	Bioengineering and Nanobiotechnologies	Good
2019	Molecular Cell Biology	Excellent
2019	Advances Practical Course in Bioorganic Chemistry	Passed
2019	Chemical Technology	Passed
2019	Genetic Engineering	Passed
2019	Current Issues and Prospects in Life Sciences (in English)	Passed
2019	Teaching Techniques and Innovative Education Technologies in Chemistry	Excellent
2020	Accomplishment and defence of of final qualifying paper	Excellent
2020	Teaching	Passed
2020	Pre-graduation Practical Training	Excellent
2020	Technological Practical Training	Excellent
2020	Protein Structure	Passed
2020	Scientific Seminar	Passed
2020	Immunology and fundamentals of virology	Excellent
	UNIVERSITY OF DELAWARE	
2021	PRACTICAL NMR SPECTROSCOPY	A-
2021	BIOCHEMISTRY	B+
2021	INTERMEDIARY METABOLISM	A
2021	BIOCHEMISTRY SEMINAR	A
2021	SEMINAR FOR NEW STUDENTS	Passed
2022	RESEARCH ETHICS	Passed
2022	BIOCHEMICAL GENETICS	B

2022	BIOCHEMISTRY SEMINAR	A-
2022	BIOPHYSICAL CHEMISTRY	A
2022	BIOCHEMISTRY SEMINAR	Passed
2022	SPECIAL SESSION RESEARCH	Passed
2022	BIOCHEMISTRY SEMINAR	Passed
2022	RESEARCH	A
2023	BIOCHEMISTRY SEMINAR	Passed
2023	RESEARCH	A
2023	SPECIAL SESSION RESEARCH	Passed
2023	BIOCHEMISTRY SEMINAR	Passed

The following grading scheme is adopted: “excellent” is the highest possible mark, “good” is the second passing mark, “satisfactory” is the lowest passing mark, “unsatisfactory” is a failure; for pass-or-fail examination “passed” or “failed” are the possible marks. Students having about 75 percent of the "excellent" grades and no more than three "satisfactory" grades at the beginning of the 12th academic term are eligible to retake no more than three exams.

BIOGRAPHICAL SKETCH

NAME: **Rozovsky, Sharon**

eRA COMMONS USER NAME: **srozovsky**

POSITION TITLE: **Professor of Chemistry and Biochemistry**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Tel Aviv University, Tel Aviv, Israel	B.S.	08/1994	Chemistry
Columbia University, New York, NY	Ph.D.	10/2000	Physical Chemistry
Columbia University, New York, NY	Postdoctoral	12/2002	Biophysical Chemistry
University of California, Berkeley, Berkeley, CA	Postdoctoral	06/2007	Biophysical Chemistry

A. Personal Statement

My research interests are the functions and regulation of selenoproteins, a class of proteins that contain the essential trace element selenium in the form of selenocysteine, identifying the different cellular roles these proteins play, and thus establishing the different ways in which selenium impacts human health. I am particularly interested in a mechanistic understanding of the biological functions of membrane-bound selenoproteins that contribute to the sensing and resolution of stress in cells.

The contributions of my group to this overall area include the studies of the enzymatic activity of selenoprotein S and selenoprotein K, two selenoproteins that are disordered enzymes. We also devised novel methods for their production, which enabled us to characterize their enzymatic activity, redox properties, and the bonds formed by the selenocysteine. In addition, we explored their interactions with various protein partners, including viral proteins, and identified general principles underlying the ability of diverse protein classes to interact with specific segments of selenoproteins K and S. Recently, my research group has employed cryo-electron microscopy and proteomics to characterize the protein complexes of selenoproteins K and S, aiming to elucidate their cellular functions.

Our contributions also include the development of a diverse chemical biology toolbox for the preparation and investigation of membrane selenoproteins and other redox enzymes. This includes our efforts to advance expressed protein ligation and genetic code expansion for the generation of selenoproteins, the creation of chemical probes for capturing reaction intermediates, and the development of ^{77}Se NMR spectroscopy for studying sulfur and selenium sites in macromolecules. These innovations have allowed us to examine the distinctive protein environment of selenoproteins and to identify the general themes guiding their reactivity.

For over a decade, I have been actively working to enable students with disabilities to become active participants in the scientific endeavor and thereby broaden the spectrum of students in science. The associated outreach activities over the years include a unique Research Experience for Undergraduates (REU) program at the University of Delaware for students with disabilities. This REU has become a model for other universities and programs that seek to increase integration and inclusion. As a member of the American Chemical Society's Chemists with Disabilities Committee, I have developed and maintained a comprehensive website that provides a wealth of resources for students with disabilities, academic advisors, and administrators. According to the fellowship guidelines, I have completed training specifically addressing sexual and gender-based harassment.

Ongoing and recently completed projects that I would like to highlight include:

- R35GM153494

Rozovsky (PI) 08/15/24 – 07/30/29

The aim of this project is to delineate the cellular functions of ER membrane selenoproteins, particularly in the degradation of misfolded and maturation-defective proteins and their roles in responding to cellular stress.

- American Heart Association Innovative Project Award

Rozovsky (PI) 07/01/23 – 06/30/25

This project focuses on calcium flux regulation through interactions of selenos with sarcoplasmic/endoplasmic reticulum calcium ATPase.

- NSF 2150863

Rozovsky (PI) 09/01/22 – 08/31/25

This project aims to investigate the membrane-bound selenoprotein S and its interactions with other protein partners beyond the protein quality control pathway, using a proteomics-based approach.

Citations:

a Li, F., Lutz, P.B., Pepelyayeva, Y., Arnér, E.S., Bayse, C.A. & **Rozovsky**, S. (2014). Redox active motifs in selenoproteins. Proceedings of the National Academy of Sciences of the United States of America, 111(19), 6976-81. PMCID: PMC4024873. Funding: NSF CAREER MCB-1054447

b Liu, J., Chen, Q. & **Rozovsky**, S. (2017). Utilizing selenocysteine for expressed protein ligation and bioconjugation. Journal of the American Chemical Society 139(9), 3430-3437. PMCID: PMC5824972. Funding: MCB-1054447; training NIH T32GM008550; instrumentation NIH P20GM104316 and P30GM110758

c Ghelichkhani, F. Gonzalez, F.A., Kapitonova, M.A. & **Rozovsky**, S. (2023). Selenoprotein S interacts with the replication and transcription complex of SARS-CoV-2 by binding nsp7. Journal of Molecular Biology, 435(8), 168008. PMCID: PMC9911985. Funding: NIH R01 GM121607 and NSF MCB-1817651

d Serbynovskyi, V., Wang, J., Chua, E. Y. D., Ishemgulova, A., Alink, L. M., Budell, W. C., Johnston, J. D., Dubbeldam, C., Gonzalez, F. A., **Rozovsky**, S., Eng, E. T., De Marco, A., and Noble, A. J. (2024). CryoCycle your grids: Plunge vitrifying and reusing clipped grids to advance cryoEM democratization. BioRxiv 2024.01.23.576763 [Preprint]. Feb 1, 2024 [cited 2024 Feb 5]. Available from: https://doi.org/10.1101/2024.01.23.576763

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2024	Member of the Organizing Committee of the 13th International Symposium on Selenium in Biology and Medicine, Daejeon, South Korea, 2025
2024	Reviewer NIH Special Emphasis Panel for Cancer Research Workforce Diversity
2024	Reviewer American Heart Association, Cardiac Biology Basic Science Committee
2023 – present	Reviewer National Center for CryoEM Access and Training User Review Committee
2022	Professor, University of Delaware, Newark, DE
2022	Organizer of the Franklin Award Symposium on Intact Mass Spectrometry of Protein Assemblies
2022	Member of the Organizing Committee of the 12th International Symposium on Selenium in Biology and Medicine, Honolulu, Hawaii, 2022
2022	Reviewer NIH Basic Mechanism in Cancer Health Disparities Special Emphasis Panel, Oncology Basic and Translation
2021	Reviewer NIH F31/32 Fellowship, Special Emphasis Panel for Fellowships on Cell Biology, Developmental Biology and Bioengineering
2021	Reviewer Delaware Clinical and Translational Research
2019 – present	Member of the State of Delaware Radiation Authority Oversight Committee
2022 – 2024	Reviewer NSF
2018 – 2020	
2018 – present	Member, Franklin Institute Committee on Science and the Arts
2024 – present	Member, American Chemical Society Committee on Chemists with Disabilities
& 2016 – 2022	
2016 – 2022	Associate Professor, University of Delaware, Newark, DE
2013 – 2022	Co-director of Research Experience for Undergraduate Program at the University of Delaware
2008 – 2018	Co-organizer of the annual Delaware Membrane Protein Symposium
2008 – 2016	Assistant Professor, University of Delaware, Newark, DE

Honors

2021	The 2021 University of Delaware's Arts and Sciences Outstanding Advocacy Award
2019	The 2019 American Chemical Society Stanley C. Israel Regional Award for Advancing Diversity in the Chemical Sciences (co-awarded with Dr. Booksh)
2011	National Science Foundation CAREER Award, National Science Foundation
2009	University of Delaware Research Foundation Innovation Award

C. Contributions to Science

1. *Selenoproteins in the Integrated Stress Response*

A major focus of my group is on membrane-bound selenoproteins that take part in the integrated stress response. In addition to managing cellular stress, these disordered selenoproteins also play a central role in inflammation and the immune response. Working towards our goal to achieve a mechanistic understanding of these membrane-embedded enzymes that rely on selenium for executing their cellular functions, we strive to chart their enzymatic reactions and interactions with their protein partners, the associated protein structures, conformational changes, and dynamics, and ultimately their specific biological roles. At this point, we have characterized the contribution of selenocysteine to the enzymatic activity of several membrane-bound selenoproteins. We were also able to measure the redox potentials of selenoproteins, the rates at which selenylsulfide (Se-S) bonds reform, and were able to establish the tendency of selenoproteins' selenocysteine to oxidize. Furthermore, we have studied, *in vivo* and *in vitro,* the formation of shorter selenoprotein variants based on peptide bond cleavage. Most recently, we have recorded the interactions of selenoprotein S with the replication and transcription complex of SARS-CoV-2. In a continuing effort, we examine the interactions of these selenoproteins with their protein partners using mass spectrometry and structural biology.

a. Liu J., Li F. & **Rozovsky** S. (2013). The intrinsically disordered membrane protein selenoprotein S is a reductase. Biochemistry, 52(18), 3051–3061. PMCID: PMC2356620. Funding: NIH P30RR031160, P30GM103519, and NSF CAREER MCB-1054447
b. Liu J., Zhang Z. & **Rozovsky** S. (2014). Selenoprotein K form an intermolecular diselenide bond with unusually high redox potential. FEBS Letters, 588, 3311-3321. PMCID: PMC25117454. Funding: NIH P30GM103519 and NSF CAREER MCB-1054447
c. Ghelichkhani, F., Gonzalez, F.A., Kapitonova, M.A., Schaefer-Ramadan, S., Liu, J., Cheng, R. & **Rozovsky** S. (2022). Selenoprotein S: A versatile disordered protein. Archives of Biochemistry and Biophysics, 731, 109427. PMCID: PMC10026367. Funding: NIH R01 GM121607 and NSF MCB-1817651
d. Ghelichkhani, F. Gonzalez, F.A., Kapitonova, M.A. & **Rozovsky**, S. (2023). Selenoprotein S interacts with the replication and transcription complex of SARS-CoV-2 by binding nsp7. Journal of Molecular Biology, 435(8), 168008. PMCID: PMC9911985. Funding: NIH R01 GM121607 and NSF MCB-1817651

2. *New Tools for Studying Proteins with Reactive Cysteines and Selenocysteines*

My research team advanced our understanding of the role of selenium and sulfur in biology by developing a variety of reagents and methods that enable the investigation of reactive cysteines and selenocysteines in proteins. Together with our collaborators, we developed several innovative, unnatural amino acids for crosslinking applications and studies of protein interactomes. In yet another effort, we co-developed novel strategies and reagents to trap the short-lived intermediates sulfenic (S-OH) and selenenic acids (Se-OH), which play an important role in protein-based signaling. While our reagents and methods were developed with selenium-centered questions in mind, they have broad applicability in the study of various biological systems beyond selenoproteins.

a. Liu, J., Cheng, R. & **Rozovsky**, S. (2018). Synthesis and semi-synthesis of selenopeptides and selenoproteins. Current Opinion in Chemical Biology 46, 41-47. PMCID: PMC6195835. Funding: NIH GM121607 and NSF MCB-1616178
b. Scinto, S.L., Ekanayake O., Seneviratne, U., Pigga, J., Boyd, S.J., Taylor, M.T., Liu, J., am Ende, C.W., **Rozovsky** S. & Fox, J. (2019). Dual reactivity trans-cyclooctenol probes for sulfenylation in live cells enable

temporal control via bioorthogonal quenching. Journal of the American Chemical Society, 141(28), 10932-10937. PMCID: PMC6756850. Funding: NIH R01 GM121607 and NSF MCB-1616178; instrumentation: NIH P20GM104316 and P30GM110758

c. Liu, J., Cao, L., Klauser, P. C., Cheng, R., Berdan, V. Y., Sun, W., Wang, N., Ghelichkhani, F., Yu, B., **Rozovsky**, S. & Wang, L. (2021). A genetically encoded fluorosulfonyloxybenzoyl-l-lysine for expansive covalent bonding of proteins via SuFEx chemistry. Journal of the American Chemical Society, 143(27), 10341-10351. PMCID: PMC8310613. Funding: NIH R01 GM121607

3. *Studies of Selenium and Sulfur Sites in Proteins by ^{77}Se NMR Spectroscopy*

My research group develops ^{77}Se NMR spectrometry to probe the structure, dynamics, and function of biological macromolecules. While these efforts serve our interest in selenoproteins, the applications of these techniques extend much further because the NMR-active ^{77}Se isotope is also an excellent surrogate for sulfur, which itself has no isotope suitable for biological NMR spectroscopy. Because of this possibility for nuclei substitution, ^{77}Se NMR spectroscopy enables the study of the multifaceted roles of cysteine and methionine in enzymatic reactions, metal binding, and molecular recognition that underpin sulfur's critical role in proper protein structure and function. Our efforts solved both major problems that had previously stifled the routine use of ^{77}Se to study proteins: The lack of straightforward procedures to enrich proteins with the NMR-active ^{77}Se and the challenges of interpreting the NMR data. To that end, we developed several facile and cost-effective methods for isotopically enriching selenoproteins by ^{77}Se. This, in turn, enabled us to start systematic ^{77}Se-NMR studies on macromolecules that established the range of chemical shifts and the ability to follow chemical reactions in selenium-rich proteins. We built a biologically relevant library of NMR parameters of selenium-containing proteins that are now available to the community as references for the analysis of ^{77}Se-NMR spectra to unlock their information content. Further expanding the ability of ^{77}Se-NMR, we recently mapped the local environment of a selenium site using distance measurements between ^{77}Se and nearby ^{13}C atoms. Consequently, ^{77}Se NMR can now be used to study recognition, binding, and conformational mobility in biological systems.

a. Schaefer, S.A., Dong, M., Rubenstein, R.P., Wilkie, W.A., Bahnson, B.J., Thorpe, C. & **Rozovsky**, S. (2013). ^{77}Se enrichment of proteins expands the biological NMR toolbox. Journal of Molecular Biology, 425(2), 222-231. PMCID: PMC3540199. Funding: NIH P30RR031160, P30GM103519, and NSF CAREER MCB-1054447; training NIH T32GM008550; instrumentation NIH P20GM104316 and P30GM110758

b. Chen, Q., Xu, S., Lu, X., Boeri, M., Pepelyayeva, Y., Diaz, E., Soni, S., Allaire, M., Forstner, M.B., Bahnson, B. & **Rozovsky**, S. (2020). ^{77}Se NMR probes the protein environment of selenomethionine. Journal of Physical Chemistry B, 124(4), 601-616. PMCID: PMC8088340. Funding: NSF MCB-1616178; training NIH T32GM008550; instrumentation: NIH P30GM110758 and GM110758

c. Quinn, C.M., Xu, S., Hou, G., Chen, Q., Sail, R., Byrd, A. & **Rozovsky**, S. (2022). ^{77}Se-^{13}C based dipolar correlation experiments to map selenium sites in microcrystalline proteins. Journal of Biomolecular NMR, 76(1-2), 29-37. PMCID: PMC9195563. Funding: NSF MCB-1616178; training NIH T32GM133395; instrumentation: NIH P20GM104316 and P30GM110758

d. Janusz Koscielniak, Jess Li, Deepak Sail, Rolf Swenson, Clemens Anklin, Sharon **Rozovsky** and R. Andrew Byrd. Exploring sulfur sites in proteins via triple-resonance ^{1}H-detected ^{77}Se NMR. *Journal of the American Chemical Society* 145, 45, 24648-24656 (2023) PMCID: PMC10655107 Funding: NIH R01 GM121607 and NSF MCB-1817651

4. *Methods Enabling Preparation and Modification of Selenoproteins*

A significant challenge to selenoprotein studies is their low cellular abundance due to the low flux of the specialized biosynthetic pathway that incorporates selenocysteine into proteins. Turning the often-problematic high reactivity of selenocysteine into an asset for engineering proteins, we exploited it for the ligation of expressed protein fragments. Among the many benefits of this method are its ability to prepare otherwise challenging proteins, its capacity to accomplish complicated ligations, and the significant increase in yield compared to other methods. Furthermore, because the method can be applied in a stepwise fashion, it enables the preparations of large proteins by multi-step ligations where several protein fragments are combined into functional proteins. These preparation strategies not only permit the production of otherwise hard-to-obtain or toxic proteins but can also be used to site-specifically attach bioconjugates.

In a different approach to selenoprotein preparation and modification, unnatural amino acids are first incorporated into proteins *in vivo* and then subsequently modified via specific, bio-orthogonal chemistries. This method based on the expansion of the genetic code was fruitfully explored in my collaboration with Dr. Wang from UCSF. There, a precursor of selenocysteine was developed that, once integrated into a target protein, can be turned into selenocysteine via a palladium-mediated cleavage under mild conditions. The initial protein containing an unnatural amino acid is thus turned into a proper selenoprotein. In an extension of this work also a precursor of cysteine was developed that allows for the controlled conversion into cysteine. In both systems, the generation of the desired final protein can be triggered on command and thus at any experimentally desired point in time.

a Liu, J., Chen, Q. & **Rozovsky**, S. (2017). Utilizing selenocysteine for expressed protein ligation and bioconjugation. Journal of the American Chemical Society, 139(9), 3430-3437. PMCID: PMC5824972. Funding: NSF CAREER MCB-1054447 and MCB-1616178; training NIH T32GM008550; instrumentation NIH P20GM104316 and P30GM110758

b Liu, J., Zheng, F., Cheng, R., Li, S., **Rozovsky**, S., Wang, Q. & Wang, L. (2018). Site-specific incorporation of selenocysteine using an expanded genetic code and palladium-mediated chemical deprotection. Journal of the American Chemical Society, 140(28), 8807-8816. PMCID: PMC6082430. Funding: NSF MCB-1616178

c Liu, J., Cheng, R., Wu, H., Li, S., Wang, P.G., DeGrado, W.F, **Rozovsky**, S. & L. Wang. (2018). Building and breaking bonds via a compact S-propargyl-cysteine to chemically control enzymes and modify proteins. Angewandte Chemie, 57(39) 12702-12706. PMCID: PMC6169525. Funding: NIH R01 GM121607 and NSF MCB-1616178

d Cheng, R., Liu J., Daithankar, V. & **Rozovsky**, S. (2022). Applying selenocysteine-mediated expressed protein ligation to prepare the membrane enzyme selenoprotein S. Methods in Enzymology 662, 159-185. PMCID: PMC9126641 Funding: NIH R01 GM121607 and NSF MCB-1616178; instrumentation NIH P20GM104316 and P30GM110758

5. *Gaining a Mechanistic Understanding of the Fundamental Properties of Selenoproteins*

Selenoproteins are crucial for the survival of organisms under stress despite their low numbers in any genome. Their unique physiochemical properties, such as low pKa, high nucleophilicity, high polarizability, and low redox potential, give them high catalytic efficiencies. However, most selenoproteins have Cys-containing homologues, and the advantages of selenocysteine in proteins remain unknown. Our group's research aims to understand selenoproteins' behavior and elucidate general properties that drive their functionality. We compare selenocysteine's behavior in different protein environments, activation by redox motifs, ability to resist damage by oxidants, and the rate of conformational switching through the formation of selenylsulfide (Se-S) or diselenide (Se-Se) bonds. Through a systematic approach to these comparisons, we are beginning to see more general themes and attributes of selenoproteins emerge.

a Liu J. & **Rozovsky** S. (2013). The contribution of selenocysteine to the peroxidase activity of selenoprotein S. Biochemistry **52** (33), 5514–5516. PMCID: PMC3809988. Funding: NSF CAREER MCB-1054447

b Li, F., Lutz, P.B., Pepelyayeva, Y., Arnér, E.S., Bayse, C.A. & **Rozovsky**, S. (2014). Redox active motifs in selenoproteins. Proceedings of the National Academy of Sciences of the United States of America, 111(19), 6976-81. PMCID: PMC4024873. Funding: NSF CAREER MCB-1054447

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