BIOGRAPHICAL SKETCH

NAME: Mukhina, Maria

eRA COMMONS USER NAME: MMUKHINA

POSITION TITLE: Assistant Professor of Physics

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
ITMO University, Saint Petersburg	BS	07/2008	Technical Physics
ITMO University, Saint Petersburg	MS	07/2010	Photonics and Optical Computer Science
ITMO University, Saint Petersburg	PHD	12/2013	Optics
Harvard University, Cambridge, MA	Postdoctoral Fellow	12/2023	Cellular Biology

A. Personal Statement

My research seeks to create the full experimental cycle, in which one can measure and generate forces in the genomes of living cells, thereby gaining control over the input while detecting the response, and then perturb mechanical properties of the molecular constituents of the genome *in situ* to pinpoint their roles in directing the flow of mechanical energy across the genome. This technological platform will enable me to study *in vivo* mechanical signaling in the genome, with the **long-term career goal** to resolve the principles underlying the connection between mechanics and functional outputs of the genome. I am uniquely qualified to pursue the **research proposed in this application**, because my MS/PhD training was in the optics of semiconductor nanocrystals and microscopy, and, for my postdoctoral training, I transitioned to cellular biology to study the mechanics of chromosomes under the guidance of Dr. Nancy Kleckner, leading expert in chromosome biology.

My doctoral studies focused on new optical properties which arise in an ensemble of anisotropic semiconductor nanocrystals as a result of their spatial alignment. After receiving a PhD, I joined an international research group led by Dr. Yurii Gun'ko where I studied chiral nanocrystals. My work uncovered that the product of conventional hot-injection colloidal synthesis is a racemate of left- and right-handed nanocrystal enantiomers (Citation [d]). This finding implies that, similarly to many drugs, constituent nanocrystal enantiomers should have profound differences in their biomedical properties. The method of enatioselective phase transfer that I developed in this project has been cited 199 times and reproduced by others (e.g. [Varga K et al., doi: 10.1021/acsnano.7b03555]).Towards the end of this period, I was the principal investigator of a group of 7 people, whose projects I formulated and guided. I also administered the projects (e.g. staffing, budget, reporting). We asked how ligand chemistry affects nanoscale chirality, implemented functional chiral nano/bio interfaces, and begun testing enantioselective cellular uptake of chiral nanocrystals. This work resulted in 4 peer-reviewed publications and 1 patent. Overall, my studies in the field of nanocrystal physics prior 2017 produced 7 peer-reviewed first-author publications.

During my postdoctoral training at the Kleckner lab, I used fluorescence microscopy to investigate chromosomes from mechanical perspective. This project produced 3 peer-reviewed publications, in one of which I am the first co-author (Citation [c]). This work led me to appreciate that thinking of chromosomes as beautifully complex mechanical objects is fundamentally dependent on the existence of an instrument for measuring forces acting within chromosomes in living cells. Hence, I relied on my significant experience in nanotechnology to develop two *in vivo* force nanoprobes, both producing optical readout but through very different physical mechanisms. The development of the nanoprobes involved basic physical research which produced a first-author publication in the peer-reviewed journal (Citation [b]). For this work, I took 3 months of training in the laboratory of Dr. Paul Alivisatos at UC Berkeley whose group is a world expert in nanocrystal physics. My training included performing colloidal hot-injection synthesis of the nanocrystals. I also opted to take a course on chromosome biology taught by Dr. Kleckner at Harvard University. My role at the Kleckner lab also involved building a microscopy system with custom hardware and software (Citation [a]), which turned into a "workhorse" of the lab.

In summary, I have the expertise, leadership, training, and motivation necessary to successfully carry out the proposed research project. Also, I would like to note that in 2022 my career was on pause for a maternity leave.

Ongoing support that I would like to highlight includes:

1R35GM156895 Mukhina (PI)
National Institutes of Health / NIGMS
In Situ Force Mapping to See Mechanical Communication in Action in Genomes of Living Cells
The goal of this project is to develop force nanoprobes for measuring forces in living cells and then to use these nanoprobes to elucidate how highly heterogeneous 3D organization of the genome promotes and censors the generation, accumulation, and redistribution of forces.
Role: PI

Research Startup Fund Mukhina (PI)
University of Maryland, College Park
Research Startup Funds
The purpose of this grant is to facilitate the establishment of PI’s research program, it is provided in equal parts by the Department of Physics and the University of Maryland, College Park.
Role: PI

Citations:

a. Mukhina MV, Chang F, Kleckner NE. ScopeScript: Fast Matlab Microscope with Custom Hardware Controller. Cambridge, MA, USA: GitHub. 2022 Nov 1. DOI: 10.5281/ZENODO.10516520.
b. Mukhina MV, Tresback J, Ondry JC, Akey A, Alivisatos AP, Kleckner N. Single-Particle Studies Reveal a Nanoscale Mechanism for Elastic, Bright, and Repeatable ZnS:Mn Mechanoluminescence in a Low-Pressure Regime. ACS Nano. 2021 Mar 23;15(3):4115-4133. PubMed Central PMCID: PMC7995957.
c. Chu L, Liang Z, Mukhina MV, Fisher JK, Hutchinson JW, Kleckner NE. One-dimensional spatial patterning along mitotic chromosomes: A mechanical basis for macroscopic morphogenesis. Proc Natl Acad Sci U S A. 2020 Oct 27;117(43):26749-26755. PubMed Central PMCID: PMC7604413.
d. Mukhina MV, Maslov VG, Baranov AV, Fedorov AV, Orlova AO, Purcell-Milton F, Govan J, Gun'ko YK. Intrinsic Chirality of CdSe/ZnS Quantum Dots and Quantum Rods. Nano Lett. 2015 May 13;15(5):2844-51. PubMed PMID: 25908405.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2024 -	Assistant Professor of Physics, University of Maryland, College Park, MD, USA
2018 - 2019	Visiting Researcher, University of California, Berkeley, CA, USA
2015 - 2015	Visiting Researcher, University of Manchester, UK
2014 - 2016	Research Associate, Center of Information Optical Technologies, ITMO University, Russia
2014 - 2014	Visiting Researcher, Trinity College Dublin, Ireland

Honors

2015 - 2016	The Scholarship of the President of the Russian Federation for Young Scientists and Graduate Students, National Council for the Support of Young Scientists of Russia
2015 - 2016	ITMO Grant for Young Scientists, ITMO University
2015 - 2015	Researcher Links Travel Grant, British Council

Other Experience

Reviewer for the following peer-reviewed journals:

Nano Letters, ACS Nano, Science Advances, Chirality, Journal of Materials Chemistry C, Journal of Physical Chemistry, Chemistry of Materials, Nano Research, Analytica Chimica Acta, Materials Advances, Scientific Reports, Laser and Photonics Reviews, Advanced Optical Materials

C. Contribution to Science

1. **Micron-scale mechanical stress patterns coincide with onset of segregation in mitotic chromosomes.** Cells employ multiple levels of organization to compact 2 m of DNA constituting a diploid human genome into the cell nucleus. Naturally, this process can be expected to lead to an emergence of complex mechanics. As a postdoc at the Kleckner lab, I participated in the work, which elucidated the output of mitotic chromosome segregation in connection to the mechanical deformations arising within DNA and DNA-binding proteins, a point of view that remains quite unique in the field. Using conventional fluorescence microscopy, my co-authors showed that segregation of mitotic chromosomes is closely follows the onset and progression of *micron-scale* mechanical patterning in both chromatin and the protein axes tightly connecting sister chromosomes. I provided a mathematical definition to these mechanical patterns, identifying them as multiple helical perversions (Citation [b] below). These patterns indicate the presence of chromosome-wide mechanical communication and hint at its roles in genome function. Overall, this work introduces new framework of thinking about mechanical effects in chromatin, which occur on the scales way larger than the size of individual constituent proteins, and as such inherently insensitive to local biochemical alterations in chromatin and, thus, purely mechanical in nature.

   The results described above have proven that conventional fluorescence microscopy can be a valuable tool to study the morphology of chromosomes, which is likely shaped by the mechanical stress. Nonetheless, this method can only produce indirect evidence for the existence of *in vivo* mechanical effects, as it does not provide mechanical readout. This realization inspired me to develop the nanoprobes that enable measuring *in vivo* forces with a nanoscale precision and across length scales ranging from nanometers to microns. Two strategies that I am developing are described in Contributions 2 and 3.

   a. Chu L, Zhang Z, Mukhina M, Zickler D, Kleckner N. Sister chromatids separate during anaphase in a three-stage program as directed by interaxis bridges. Proc Natl Acad Sci U S A. 2022 Mar 8;119(10):e2123363119. PubMed Central PMCID: PMC8915976.
   b. Chu L*, Liang Z*, Mukhina MV*, Fisher JK, Hutchinson JW, Kleckner NE. One-dimensional spatial patterning along mitotic chromosomes: A mechanical basis for macroscopic morphogenesis. Proc Natl Acad Sci U S A. 2020 Oct 27;117(43):26749-26755. PubMed Central PMCID: PMC7604413.
   **These authors contributed equally to this work*
   c. Chu L, Liang Z, Mukhina M, Fisher J, Vincenten N, Zhang Z, Hutchinson J, Zickler D, Kleckner N. The 3D Topography of Mitotic Chromosomes. Mol Cell. 2020 Sep 17;79(6):902-916.e6. PubMed Central PMCID: PMC7502541.

2. **Discovery of the nanoscale mechanism of mechanoluminescence in ZnMnS that opens a pathway to intracellular mechanoluminescent force nanoprobes.** In mechanoluminescence (ML), a crystal deformed as a result of force application produces photons, thus serving as a force sensor with a direct optical readout. To implement the ML nanoprobes, I first needed to explore ZnMnS, a material, which I identified as a promising candidate for the ML sensor. For this work, I first spent 3 months in the laboratory of Prof. Paul Alivisatos at UC Berkeley whose group is a world expert in nanocrystal synthesis. This work led me to appreciate that the mechanism of ZnMnS ML, while widely discussed, was in fact unclear and that further understanding was required for successful use of this material. Upon returning to Harvard, I carried out studies of ML in single ZnMnS *micro*particles, which identified stacking faults, a nanoscale structural defect, as vital for ML in this material (Citation [a] below). This finding resolved fundamental paradoxes in the field. I concomitantly showed that this ML operates at excitation pressures between 0.2 and 47 pN/nm^2, i.e. in the range of intracellular forces. With this knowledge in hand, I have engaged in a collaboration with Raymond Schaak laboratory to synthesize nanorods small enough for *in vivo* use and having the stacking faults that I predicted to be essential for ML. I then used a single-particle correlational AFM and optical microscopy to show that these nanorods do indeed exhibit exceptionally bright ML, with 45-fold increase over analogous nanocrystals without stacking faults, thus setting the stage for disruptive *in vivo* force sensing technology, free from autofluorescence background and phototoxicity.

a. Mukhina MV, Tresback J, Ondry JC, Akey A, Alivisatos AP, Kleckner N. Single-Particle Studies Reveal a Nanoscale Mechanism for Elastic, Bright, and Repeatable ZnS:Mn Mechanoluminescence in a Low-Pressure Regime. ACS Nano. 2021 Mar 23;15(3):4115-4133. PubMed Central PMCID: PMC7995957.
b. Mukhina M, Young H, McCormick C, Butterfield A, Schaak R, Kleckner N. Nanoscale mechanoluminescence excitation in faulted ZnMnS nanorods. ACS Nano, under review. 2025.

3. **DNA-origami based nanoprobes for real-time force mapping in genomes of living cells.** Complimentary to the ML nanoprobes, I utilized well-established DNA origami technology to create dynamic DNA nanostructure, which reports applied force by switching between the open and closed states with different cumulative color of photoexcited luminescence. I have demonstrated that these nanoprobes can be covered with protective polymer coating for *in vivo* stability and delivered to the nucleus *via* microinjection or electroporation assisted by Nuclear Localization Signal (NLS) peptides. I then used CuAAC click chemistry to attach the origami force nanoprobes to nuclear DNA non-loci-specifically to produce a micron-scale map of compressive forces with a nanoscale precision (~ 100 nm, the size of the probe). The results of this project have been presented at the APS annual meeting and are being prepared for publication.

   a. Mukhina M, Tsai V, Gromova Yu, Kleckner N. *In Situ* Observation of Compressive Forces Experienced by DNA Loci in the Nucleus of Living HeLa Cell. APS Global Summit; 2025 March 20.

4. **Microscope with custom hardware and software for fast imaging and mechanical stimulation**. Concomitant with the nanoprobe studies, I built an optical microscopy system with the capacity to integrate 7 automatic controls (x, y, z, time, wavelength, multiple xy locations, mechanical deformation). Custom software and hardware allow to apply mechanical deformation and record induced optical response with sub-millisecond temporal resolution of 1580 fps. The software package alongside the design files for the microscope controller are made publicly available through publishing in GitHub repositories (Citation [a]). The above setup had been used to obtain recordings of a single mechanoluminescence pulses (Contribution 2 above) with temporal resolution of 633 µsec, thus providing direct evidence that the mechanoluminescence was emitted from stacking faults (Fig. 4 of Citation [b] below).

   a. Mukhina M, Chang F, Kleckner N. ScopeScript: Fast Matlab Microscope with Custom Hardware Controller. Cambridge, MA, USA: GitHub; 2022 November. DOI: 10.5281/ZENODO.10516520
   b. Mukhina MV, Tresback J, Ondry JC, Akey A, Alivisatos AP, Kleckner N. Single-Particle Studies Reveal a Nanoscale Mechanism for Elastic, Bright, and Repeatable ZnS:Mn Mechanoluminescence in a Low-Pressure Regime. ACS Nano. 2021 Mar 23;15(3):4115-4133. PubMed Central PMCID: PMC7995957.

D. Publications [h-index 14, 5 most cited papers are highlighted]

Complete list of published work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/maria.mukhina.1/bibliography/public/

‡**Mukhina M**, Young H, McCormick C, Butterfield A, Schaak R, Kleckner N. Nanoscale mechanoluminescence excitation in faulted ZnMnS nanorods. ACS Nano, under review (2025)

Invited paper: **Maria Mukhina**. Bringing Chiral Functionality to In Vivo Applications of Nanomaterials. Light: Science & Applications, 11 (157) (2022)

Lingluo Chu, Zheng Zhang, **Maria V. Mukhina**, Denise Zickler, Nancy E. Kleckner. Sister chromatids separate during anaphase in a three-stage program as directed by inter-axis bridges. PNAS, 119 (10), e2123363119 (2022)

[50 citations] *Highlighted in ACS monthly feature In Nano*: ‡**Maria V. Mukhina**, Jason S. Tresback, Justin C. Ondry, Austin Akey, A. Paul Alivisatos, and Nancy Kleckner. Single particle studies reveal a new mechanism for elastic, bright, and repeatable ZnS:Mn mechanoluminescence in a low pressure regime. ACS Nano, 15 (3) 4115-4133 (2021)

‡Lingluo Chu*, Zhangyi Liang*, **Maria Mukhina***, Jay K. Fisher, John Hutchinson, Nancy Kleckner. One-dimensional spatial patterning along mitotic chromosomes: a mechanical basis for macroscopic morphogenesis. PNAS, 117 (43) 26749-26755 (2020)
**These authors contributed equally to this work*

Lingluo Chu, Zhangyi Liang, **Maria Mukhina**, Jay Fisher, Nadine Vincenten, Zheng Zhang, John Hutchinson, Denise Zickler, Nancy Kleckner. The 3D Topography of Mitotic Chromosomes. Molecular Cell, 79, 1–15 (2020)

‡**Maria V Mukhina,** Anvar S Baimuratov, Ivan D Rukhlenko, Vladimir G Maslov, Finn Purcell Milton, Yurii K Gun'ko, Alexander V Baranov, Anatoly V Fedorov. Circular Dichroism of Electric-Field-Oriented CdSe/CdS Quantum Dots-in-Rods. ACS Nano, 10, 8904-8909 (2016)

[54 citations] ‡**Maria V Mukhina**, Ivan V Korsakov, Vladimir G Maslov, Finn Purcell Milton, Joseph Govan, Alexander V Baranov, Anatoly V Fedorov, Yurii K Gun'ko. Molecular Recognition of Biomolecules by Chiral CdSe Quantum Dots. Scientific Reports, 6, 24177 (2016)

[138 citations] Finn Purcell-Milton, Joseph Govan, **Maria V Mukhina,** and Yurii K. Gun'ko. The chiral nano-world: chiroptically active quantum nanostructures. Nanoscale Horizons, 1, 14-26 (2016)

Maria V Mukhina, Vladimir G Maslov, Ivan V Korsakov, Finn Purcell Milton, Alexander Loudon, Alexander V Baranov, Anatoly V Fedorov, Yurii K Gun'ko. Optically active II-VI semiconductor nanocrystals via chiral phase transfer. MRS Proceedings, 1793, mrss15-2125910 (2015)

[212 citations] ‡**Maria V. Mukhina**, Vladimir G. Maslov, Alexander V. Baranov, Anatoly V. Fedorov, Anna O. Orlova, Finn Purcell-Milton, Joseph Govan, and Yurii K. Gun'ko. Intrinsic Chirality of CdSe/ZnS Quantum Dots and Quantum Rods. Nano Letters, 15 (5), 2844-2851 (2015)

[145 citations] Mícheál P Moloney, Joseph Govan, Alexander Loudon, **Maria Mukhina**, Yurii K Gun'ko. Preparation of chiral quantum dots. Nature Protocols, 10(4) 558-573 (2015)

Igor I. Shaganov, Tatiana S. Perova, **Maria V. Mukhina,** Irina V. Martynenko, Alexander V. Baranov, Anatoly V. Fedorov, Valerie Gerard, Yuri K. Gun'ko. Influence of intermolecular interactions on spectroscopic characteristics of metal nanoparticles and their composites. Physical Chemistry Chemical Physics, 16, 24536 (2014)

M.V. Mukhina, V.G. Maslov, A.V. Baranov, A.V. Fedorov. Selective photochemical reaction in an ensemble of CdSe/ZnS quantum rods. Optical Engineering, 53(8) 087107-(1-6) (2014)

M.V. Mukhina, V.G. Maslov, A.V. Baranov, A.V. Fedorov. Photoinduced polarized luminescence enhancement and darkening in an ensemble of CdSe/ZnS quantum rods. Proceedings of SPIE, 9126 912620-(1-10) (2014)

M.V. Mukhina, V.G. Maslov, A.V. Baranov, M.V. Artemyev, A.V. Fedorov. Anisotropic absorption of CdSe/ZnS quantum rods embedded in polymer film. Advances in Nano Research, 1(3) 153-158 (2013)

M.V. Mukhina, V.G. Maslov, A.V. Baranov, M.V. Artemyev, A.O. Orlova, A.V. Fedorov**.** Anisotropy of optical transitions in ordered ensemble of CdSe quantum rods. Optics Letters, 38(17) 3426-3428 (2013)

M.V. Mukhina, V.G. Maslov, A.V. Baranov, A.V. Fedorov**,** K. Berwick. Photoinduced anisotropy in an ensemble of CdSe/ZnS quantum rods. RSC Advances, 3 20746-20749 (2013)

M.V. Mukhina, V.V. Danilov, A.O. Orlova, A.V. Fedorov, M.V. Artemyev, A.V. Baranov. Electrically controlled polarized photoluminescence of CdSe/ZnS nanorods embedded in a liquid crystal template. Nanotechnology, 23(32) 325101(1-6) (2012)