

# Mirkó Palla, PhD



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## CAREER OBJECTIVE

My goal is to work in an innovative and interdisciplinary academic research environment, specializing in novel biomedical instrumentation and technology development to advance medical diagnostics using single molecule sensing and actuation techniques.

## RESEARCH INTERESTS

- High-throughput, single molecule DNA sequencing / synthesis / editing technologies
- Bionano instrumentation in medicine, novel medical devices, BioMEMS
- Relationship between biological system responses and physical, chemical mechanisms

## EDUCATION

**2014-2019**

**Harvard University** – Boston, MA

Postdoctoral Fellow, Wyss Institute of Biologically Inspired Engineering

Department of Genetics, Harvard Medical School

Advisor: Professor George M. Church

Research Focus:

Development of a novel, integrated circuit based ionic current blockade detector enabling massively parallel single-molecule (SM) DNA sequencing, combining the advantages of sequencing by synthesis with the speed and sensitivity of the biological  $\alpha$ HL nanopore. Special focus on SM data analysis to categorize and uniquely discriminate current blockade signals of individual bases collected during real-time measurements.

**2008-2014**

**Columbia University** – New York, NY

Doctor of Philosophy (2014), Department of Mechanical Engineering

Advisor: Professor Jingyue Ju

Dissertation: “*Novel Engineering Approaches for DNA Sequencing and Analysis*”

Master of Philosophy (2012), Master of Science in Mechanical Engineering (2010)

GPA: 3.82/4.00

Advanced Courses:

Advanced Heat Transfer, Advanced Manufacturing Processes, Advanced Mechanics of Fluids, Case Studies in Computational Fluid Dynamics, Complex Variables, Control Theory, Genomic Information Science and Technology, Genome Sequencing Laboratory, Molecular Mechanics, Numerical Methods, Theory of Elasticity

**2005-2007**

**Clarkson University** – Potsdam, NY

Bachelor of Science with Great Distinction, Department of Mechanical Engineering

Minor in Mathematics; Presidential Scholar (2005-2007), Dean’s List (Fall 2006)

GPA: 3.92/4.00 – top of the class

Advanced Courses:

Dynamical Systems, Finite Element Analysis, Integrated Design, Mechanical Vibrations and Control, Principles of Microeconomics, Thermodynamic System Engineering

Scholarship: Honors and International Scholar

**2005-2006**     **Harvard University** – Cambridge, MA  
Graduate course: Computational and Functional Genomics, Biophysics Program

**2002-2005**     **State University of New York College at Potsdam** – Potsdam, NY  
Double Major: Physics and Mathematics; Minor: Computer Science  
Basic coursework in Liberal Arts Studies  
GPA: 3.95/4.00

Advanced Courses:

Advanced Scheme, Analysis of Algorithms, Discrete Data Structures, Finite Fields,  
Quantum Physics, Programming Structures, Theory of Sets

## AWARDS AND DISTINCTIONS

### Harvard University

- Financial award recipient from the Aspen Center for Physics (ACP) to present at the 10th Biennial Workshop on Single Molecule Biophysics (SMB2019) in Aspen, CO
- Best Poster Award at the 2017 Annual Genetics Retreat of Harvard Medical School
- Travel grant recipient from the Chemical and Biological Microsystems Society (CBMS) to present at the 20th International Conference on Miniaturized Systems for Chemistry and Life Sciences (MicroTAS 2016) in Dublin, Ireland
- Technical Programme Committee nominee for the special issue of the IEEE Sensors Journal: “Selected Papers from the 2015 IEEE Sensors Conference” – top 10% of conference proceedings

### Columbia University

- Graduate Research Assistant Award with full tuition coverage during Master’s phase (2010-2012)

### Clarkson University

- Norman L. Rea Award for Excellence in Mechanical Engineering (2007)
- Clarkson University Honors and International Scholarship Recipient (2005-2007)

### SUNY Potsdam

- Received Presidential Scholar Research Grant in Bioinformatics (2004)
- Winner of the Charlie Smith Award for Excellence in Mathematics (2004)
- Departmental Award for Academic Excellence in Chemistry (2003)
- Member of the Hungarian National Junior U-20 Ice Hockey Team (1997-2001)

## PROFESSIONAL ACTIVITIES AND SERVICE

- Invited reviewer, Biophysical Journal (2019-present)
- Invited judge, Annual National Collegiate Research Conference (NCRC) (2018-present)
- Reviewer for the IEEE Conference on Sensors (IEEE SENSORS) (2017-present)
- Invited reviewer, IEEE Sensors Letters (2017-present)
- Invited reviewer, IEEE Life Science Letters (2016-present)
- GSAS Harvard Biotechnology Club Member (2015-present)
- Harlem Biospace (Hb) Biotech Incubator Community Member (2014-present)
- Columbia Engineering Entrepreneurship Mentoring Program (2011-2014)
- TEDx Columbia Engineering Programming and Speaker Selection Committee (2011)

- Columbia University Men's Hockey Team (2008-2011)
- Honors Program (SUNY-Potsdam: 2002-2005; Clarkson University: 2005-2007)
- National Honor Societies: Phi Eta Sigma (Freshman), Sigma Pi Sigma (Physics), Pi Mu Epsilon (Mathematics), Pi Tau Sigma (International Mechanical Engineering Honor Society), Tau Beta Pi (Engineering Honor Society)
- Professional Societies: Institute of Electrical and Electronics Engineers (IEEE), American Chemical Society (ACS), Society of Physics Students (SPS), Association for Computing Machinery (ACM), American Society of Mechanical Engineers (ASME)

## TEACHING AND MENTORING EXPERIENCE

### 2016-2019 Postdoctoral Supervisor

Department of Genetics, Harvard Medical School – Boston, MA

Guided visiting postdoctoral researcher (Valentin Dubois) in the design and characterization of a solid-state nanopore array for single molecule DNA sequencing. (September 2017 – present)

Mentored postdoctoral research fellow (Sukanya Punthambaker) in the development of a multiplex screening tool to identify variants with novel properties for applications of biotechnological interest. (September 2016 – present)

### 2015-2016 Research Assistant Supervisor

Wyss Institute of Biologically Inspired Engineering – Boston, MA

Directed research assistant (Daniel Wiegand) in the development of a differential equation-based, quantitative statistical model to predict oligonucleotide assembly reaction kinetics in gene synthesis. Mentee has been accepted to the Chemical Engineering PhD program at Northeastern University. (March 2015 – December 2016)

Managed research assistant (Michael Tung) in the implementation of a novel sequencing method by the integration of super-resolution microscopy, physical DNA stretching and structural ligation of DNA origami barcodes. Mentee has transitioned to the Bioinformatics Master's program at Boston University. (May 2014 – February 2015)

### 2014-2015 Minority Access Program (MAP) Mentor

Department of Genetics, Harvard Medical School – Boston, MA

Supervised undergraduate summer student (Abbas Adris) in the implementation of a coarse-grain simulation model to optimize a linker-based protein attachment strategy for single molecule DNA sequencing. (May 2015 – August 2015)

Mentored undergraduate summer student (Aman Aberra) in the development of a profile-based base-caller for single molecule DNA sequencing. Mentee later became an NSF Fellow. (May 2014 – August 2014)

### 2012-2014 Undergraduate Mathematics Tutor

Columbia University – New York, NY

Taught undergraduate students one-on-one in an introductory statistic course by preparing them for quizzes, midterms and final examinations. (February 2012 – February 2014)

- 2005-2007 Collegiate Science and Technology Entry Program (CSTEP) Tutor**  
Clarkson University – Potsdam, NY
- Instructed and tutored students in courses of the Mechanical Engineering curriculum such as Fluid Mechanics, Finite Element Analysis, Mechanical Vibrations and Control, and Heat Transfer. (January 2005 – May 2007)
- 2004-2005 Coordinator/Counselor**  
CSTEP Jumpstart Summer Program, SUNY Potsdam – Potsdam, NY
- Planned and implemented pre-college sessions for incoming freshmen in science. (June 2004 – August 2004)
- 2003-2005 Physics Teaching Assistant**  
Department of Physics, SUNY Potsdam – Potsdam, NY
- Responsible for departmental problem sets, exam and lab assignment grading. Assisted lab component of class, emphasizing complete and accurate scientific note taking. (August 2004 – January 2005)
- Computer Science Teaching Assistant**  
Department of Computer Science, SUNY Potsdam – Potsdam, NY
- Graded homework assignments and assisted students with their projects or material they found difficult to understand. (May 2003 – January 2005)
- Peer Tutor in Mathematics**  
Student Success Center, SUNY Potsdam – Potsdam, NY
- Responsible to help individual students to achieve higher academic results in a drop-in learning center. (August 2003 – January 2005)

## ENTREPRENEURSHIP

### **Tech Xperience Week - Brainport Eindhoven**

Eindhoven, The Netherlands

Selected as one of the top 10 candidates of high-tech talents from 500 international applicants to participate in a fully paid week to explore the Brainport Eindhoven region. Visited companies and research institutes (Philips, Fujifilm, Holst Centre, Vanderlande, VDL Group, ASML) and learned about their current developments, innovations and working culture during meetings with employees and representatives. Also attended lectures and solved specific case studies with fellow participants and employees in small group settings (October 2018).

### **Hacking Farming Co-Creation Sprint 2017 - Bayer Crop Science**

Bayer LifeHub – Cambridge, MA

Winner of a 3-day, interdisciplinary team-based consulting competition on the topic of seed sorting – a global challenge. In a small-team setting, mentored by a Bayer industry expert, designed and implemented a scalable, electrostatic seed separation method. After multiple prototyping iterations, pitched a finalized technical solution in form of a demo and oral presentation for a panel of real-world experts in the field of agriculture. (September 2017).

### **8th Annual Harvard vs. MIT Case Competition - Harvard Graduate Consulting Club (HGCC)**

Harvard University | Massachusetts Institute of Technology – Boston, MA

Competed in a 2-week, fast-paced consulting event to address a real-life business challenge posed by Merrimack Pharmaceuticals, a company that develops therapies and treatment of diseases in the areas of autoimmunity and cancer. In a randomized, 4-person team setting, mentored by consultants and industrialists, proposed an optimal 3-year pricing strategy for an antibody-based drug of novel EGFR inhibitors for colorectal cancer treatment. Focusing on the US market, developed a value-based solution acknowledging balance between profitability and patient benefit, and the complexity of pricing of pharmaceutical drugs considering the full spectrum of stakeholders. (July 2016)

### **Grand Hack - MIT Hacking Medicine**

MIT Media Lab, Massachusetts Institute of Technology – Boston, MA

Self-assembled an interdisciplinary team composed of medical doctors, engineers, scientist, health professionals, software developers and business-oriented personnel. As a team, formulated a real-world problem focused on monitoring patient progress with chronic disease (such as diabetes), implemented an easy-to-use smartphone-based application to motivate and track health records dynamically personalized to the patient interaction activity, and finally pitched this business idea in front of a panel of VCs and health professional experts. (April 2015)

## **CAREER DEVELOPMENT**

### **Funding Your Research: NIH Course - The Harvard Catalyst Education Program**

Harvard University – Boston, MA

Completed a 5-week online course, accredited by the Massachusetts Medical Society, which provided an overview of the NIH grant submission process, with a particular focus on the R01 and K career development grants. Topics explained how to develop a fundable research topic, practice effective project management, work with grant administrators and collaborators to assemble the grant, and navigate the NIH peer review process. (June 2018)

### **Leadership Strategies for the Researcher Course - The Harvard Catalyst Education Program**

Harvard University – Boston, MA

Completed a 2-day, intensive course, accredited by the Massachusetts Medical Society, which featured both interactive and didactic sessions, with a focus on best practices in leading and managing a team, and navigating a career path in research. Session topics detailed how to develop a personal strategy, manage grant finances, effectively use communication styles, resolve conflict, and hire, manage, and terminate team members. (June 2018)

### **Funding Your Research: Non-NIH Governmental Agencies Course - The Harvard Catalyst Education Program**

Harvard University – Boston, MA

Completed a 5-week online course, accredited by the Massachusetts Medical Society, which explored the availability of medical research funding beyond the NIH. Topics covered included the grant submission process, with examples drawn from agencies of NSF, Patient-Centered Outcomes Research Institute (PCORI) and DoD. Learn lessons from professors who have successfully acquired these types of grants. (May 2018)

### **Effectively Communicating Research Course - The Harvard Catalyst Education Program**

Harvard University – Boston, MA

Completed a 2-day, intensive course, accredited by the Massachusetts Medical Society, which was designed to provide fellows and junior faculty with the skills necessary to express their science clearly to diverse audiences; to prepare abstracts, manuscripts, and posters, and to speak effectively.

With the guidance and expertise of the course faculty, including journal editors and leading scientists, acquired tools necessary to convey science effectively. (October 2017)

### **Successful Grant Writing Strategies Course - The Harvard Catalyst Education Program**

Harvard University – Boston, MA

Completed a 5-week online course, accredited by the Massachusetts Medical Society, on scientific grant writing. The course provided information on the preliminary components needed to apply for funding, with special emphasis on the importance of clear communication of the major grant ideas. Learned about the basic construction of a grant, the budget process and the general peer review process with implications of the final decision. (May 2017)

### **Patent Law Essentials Workshop - The Independent Activities Period (IAP)**

Stata Center, Massachusetts Institute of Technology – Cambridge, MA

Completed a 4-hour interactive workshop covering the basics of U.S. patent law, including the patent application process, prosecution, litigation and licensing. Learned about recent developments in patent law specifically for inventors and examples ranging from the computer software to the pharmaceutical industries. (January 2017)

### **Healthcare Innovation & Commercialization Course (HIC)**

Armenise Auditorium, Harvard Medical School – Boston, MA

Participated in a 10-week hands-on workshop led by accomplished entrepreneurs, venture capitalists, corporate executives, and experts who are closely involved in commercializing innovations in healthcare. Learned about industry trends in the life sciences, regulatory and reimbursement issues, health policy, startups and startup financing, venture capital, licensing and technology transfer process from academia to industry. After selecting a current Harvard technology [DNA nano-origami capsule for targeted drug delivery], in a small team setting, investigated its market potential and developed a roadmap for a successful product launch during an 8-week period. Finally, in the form of a 3-minute venture capital pitch, presented the problem, market opportunity and solution to the technology in development. (September 2016)

### **Medical Device Development Course - The Harvard Catalyst Education Program**

Joseph B. Martin Conference Center, Harvard Medical School – Boston, MA

Completed a 2-day intensive course, accredited by the Massachusetts Medical Society, on medical device development and translation. Designed for clinical and translational researchers, the course provided an opportunity to explore and navigate the principles underlying the challenges of medical device and diagnostics development, with special focus on technology transfer, the regulatory process and commercialization. Gained knowledge on how to identify clinical need, evaluate and validate novel technologies, improve on existing medical devices and technologies and conduct pre-clinical and clinical studies and post-market surveillance. (May 2016)

### **IARPA/SRC Workshop on DNA-based Massive Information Storage**

Senate Ballroom, Hyatt Arlington – Arlington, VA

This invitation-only workshop explored the near-term feasibility of developing a massive information storage technology based on DNA organizing principles. In an interactive framework, it encouraged exploratory thinking with a goal of supporting an aggressive DNA-based memory system development cycle. Leading questions were offered to stimulate discussion for each of the workshop topical areas and these were followed by a set of straw five-year development objectives. (April 2016)

## GRANT WRITING CONTRIBUTIONS

Grant Number: R01 RFA-HG-18-001 | Project Date: 4/1/2019 - 3/31/2023 | Submitted  
Proposed Amount: **\$2,653,111**  
Funding Agency: National Human Genome Research Institute, National Institutes of Health  
Title: "Single-Molecule Electronic Nucleic Acid Sequencing-by-Synthesis Using Novel Tagged Nucleotides and Nanopore Constructs" (PI: J. Ju, G.M. Church)

Grant Number: IARPA-BAA-18-03 | Project Date: 01/01/2019 – 01/31/2023 | Submitted  
Proposed Amount: **\$5,251,675**  
Funding Agency: Intelligence Advanced Research Projects Activity, MIST Program  
Title: "Flexible-write information storage in DNA" (PI: G. Church, H. Lee)

Grant Number: HR001118S0023 | Project Date: 11/01/2018 – 10/31/2022 | Funded (Phase II)  
Proposed Amount: **\$1,950,004**  
Funding Agency: Defense Advanced Research Projects Agency, Biological Technologies Office  
Title: "Epigenetic CHaracterization and Observation" (PI: S.C. Sealfon, G.M. Church)

Grant Number: R01 RFA-HG-18-001 | Project Date: 10/1/2018 - 9/30/2023 | Denied  
Proposed Amount: **\$4,112,409**  
Funding Agency: National Human Genome Research Institute, National Institutes of Health  
Title: "Direct RNA Sequencing using Nanopore SBS" (PI: J. Ju, G.M. Church)

Grant Number: MCB-1445570 | Project Date: 08/01/2014 – 07/31/2017 | Completed  
Awarded Amount: **\$334,523**  
Funding Agency: Division of Molecular and Cellular Bioscience, National Science Foundation  
Title: "ERASynBio: Intensification of the Synthetic Biology Design Cycle" (PI: G.M. Church)

Grant Number: R01 HG007415-02 | Project Date: 09/01/2013 – 07/31/2016 | Completed  
Awarded Amount: **\$5,171,249**  
Funding Agency: National Human Genome Research Institute, National Institutes of Health  
Title: "An Integrated System for Single Molecule Electronic Sequencing by Synthesis" (PI: J. Ju)

Grant Number: R01 CA169620-01 | Denied  
Funding Agency: National Library of Medicine, National Institutes of Health  
Title: "An Integrated Microsystem for Multiplex Genotyping and Indel Detection" (PI: Q. Lin)

Grant Number: R01 HG006327-01A1 | Denied  
Funding Agency: National Human Genome Research Institute, National Institutes of Health  
Title: "DNA Sequencing by Synthesis using Azidomethyl Modified Nucleotide Reversible Terminators" (PI: J. Ju)

## JOURNAL PUBLICATIONS

M. Palla, David B. Thompson<sup>†</sup>, G.M. Church. (2018) Single-Molecule Characterization of a Nanopore-Coupled Cas9 Protein on an Electrode Array, **IEEE Xplore**, 8630288.

M. Palla, S. Punthambaker<sup>†</sup>, P.B. Stranges, F. Vigneault, J. Nivala, A. Ayer, T. Craig, D. Gremyachinskiy, H. Franklin, S. Sun, J. Pollard, A. Trans, A. Qwan, C.W. Fuller, S. Roeber, G.M. Church. (2018) Multiplex Single-Molecule Kinetics of Nanopore-Coupled Polymerases, **Nature Communications**, in revision.

M. Palla, Z. Li, S. Jockusch, F.G. Bosco, T. Rindzevicius, M.S. Schmidt, J.J. Russo, A. Boisen, J. Ju. (2017) Click Chemistry Based Biomolecular Conjugation Monitoring Using Surface-Enhanced Raman Spectroscopy Mapping. **IEEE Xplore**, 7808595.

P.B Stranges, M. Palla<sup>†</sup>, S. Kalachikov, J. Nivala, M. Dorwart, A. Trans, S. Kumar, M. Porel, M. Chien, C. Tao, I. Morozova, Z. Li, S. Shi, A. Aberra, C. Spilman, A. Yang, A. Aguirre, T. Harada, D. Korenblum, J. Pollard, A. Bibillo, R. Chen, R. Davis, J.J. Russo, C. Fuller, S. Roeber, J. Ju, G.M. Church. (2016) Design and Characterization of a Nanopore-Coupled Polymerase for Single Molecule DNA Sequencing by Synthesis on an Integrated Electronic Array, **PNAS**, 44, E6749–E6756.

C.W. Fuller, S. Kumar, M. Porel, M. Chien, A. Bibillo, P.B. Stranges, M. Dorwart, C. Tao, Z. Li, W. Guo, S. Shi, D. Korenblum, A. Trans, A. Aguirre, E. Liu, T. Harada, J. Pollard, J. Hu, C. Cech, A. Yang, C. Spilman, M. Palla, R. Chen, I. Morozova, S. Kalachikov, J.J. Russo, J. Kasianowicz, G.M. Church, R. Davis, J. Ju. (2016) Real-Time, Single Molecule Electronic DNA Sequencing by Synthesis on a Nanopore Array. **PNAS**, 19, 5233–5238.

M. Palla, F.G. Bosco<sup>†</sup>, J. Yang<sup>†</sup>, T. Rindzevicius, T.S. Alstrom, M.S. Schmidt, Q. Lin, A. Boisen, J. Ju. (2015) Mathematical Model for Biomolecular Quantification Using Large-Area Surface-Enhanced Raman Spectroscopy Mapping. **RSC Advances**, 5, 85845-85853.

M. Palla, W. Guo, S. Shi, Z. Li, J. Wu, S. Jockusch, C. Guo, J.J. Russo, N.J. Turro, J. Ju. (2014) DNA Sequencing by Synthesis Using 3'-O-Azidomethyl Nucleotide Reversible Terminators and Surface-Enhanced Raman Spectroscopic Detection. **RSC Advances**, 4, 49342–49346.

J. Yang, M. Palla<sup>†</sup>, F.G. Bosco<sup>†</sup>, M.S. Schmidt, A. Boisen, J. Ju, Q. Lin. (2013) A SERS-based Quantitative Bioassay on Aptamer-functionalized Nanopillars Using Large-area Raman Mapping. **ACS Nano**, 7, 5350–5359.

J. Zhu, C. Qiu<sup>†</sup>, M. Palla, J. Russo, J. Ju, Q. Lin. (2014) A Microfluidic Device for Multiplex Single Nucleotide Polymorphism Genotyping. **RSC Advances**, 4, 4269-4277.

J. Zhu, M. Palla, S. Ronca, R. Warpner, J. Ju, Q. Lin. (2013) A MEMS-based Approach to Single Nucleotide Polymorphism Genotyping. **Sensors and Actuators A: Physical**, 195, 175–182.

Y. Zhang, M. Palla, A. Sun, J.-C. Liao. (2013) Identification of Unique Interactions between the Flexible Linker and the RecA-Like Domains of DEAD-Box Helicase Mss116. **Journal of Physics: Condensed Matter**, 25, 374101.

M. Palla, C.-P. Chen, Y. Zhang, J.L. Li, J. Ju, J.-C. Liao. (2013) Mechanism of Flexibility Control for ATP Access of Hepatitis C virus NS3 Helicase. **Journal of Biomolecular Structure and Dynamics**, 31, 129-141.

## CONFERENCE PRESENTATIONS

M. Palla, S. Punthambaker, D.J. Wiegand, G.M. Church. "Single-Molecule Kinetic Screen of DNA Polymerase Libraries on a Nanopore Array" **The 10th Biennial Workshop on Single Molecule Biophysics (SMB2019)** – Aspen, CO. January 2019.

<sup>†</sup> This author contributed equally to the first author.



M. Palla, D.B. Thompson<sup>†</sup>, G.M. Church. “Single-Molecule Characterization of a Nanopore-Coupled Cas9 Protein on an Electrode Array” **The 17th IEEE Conference on Sensors (IEEE SENSORS 2018)** – New Delhi, India. October 2018.

M. Palla, D.B. Thompson<sup>†</sup>, G.M. Church. “Single-Molecule Characterization of a Nanopore-Coupled Cas9 Protein on an Electrode Array” **Gordon Research Conference on Single Molecule Approaches to Biology** – Mount Snow, VT. July 2018.

M. Palla, S. Punthambaker<sup>†</sup>, P.B. Stranges, F. Vigneault, J. Nivala, A. Ayer, T. Craig, D. Gremyachinskiy, H. Franklin, S. Sun, J. Pollard, A. Trans, A. Qwan, C.W. Fuller, S. Roever, G.M. Church. “Multiplex Single-Molecule Kinetics of Nanopore-Coupled Polymerases” **Biophysical Society 62nd Annual Meeting** – San Francisco, CA. February 2018.

M. Palla, S. Punthambaker<sup>†</sup>, P.B. Stranges, F. Vigneault, J. Nivala, A. Ayer, S. Sun, J. Pollard, A. Trans, A. Qwan, C.W. Fuller, G.M. Church. “Single Molecule Kinetic Profiling of Polymerases on a Nanopore Array” **The 21st International Conference on Miniaturized Systems for Chemistry and Life Sciences (MicroTAS 2017)** – Savannah, GA. October 2017.

M. Palla, S. Kumar, Z. Li, S. Jockusch, F.G. Bosco, T. Rindzevicius, T.S. Alstrøm, M.S. Schmidt, J.J. Russo, A. Boisen, J. Ju. “Click Chemistry Based Biomolecular Conjugation Monitoring Using Surface-Enhanced Raman Spectroscopy Mapping” **The 15th IEEE Conference on Sensors (IEEE SENSORS 2016)** – Orlando, FL. October 2016.

P.B. Stranges, M. Palla<sup>†</sup>, S. Kalachikov, J. Nivala, M. Dorwart, A. Trans, S. Kumar, M. Porel, M. Chien, C. Tao, I. Morozova, Z. Li, S. Shi, A. Aberra, C. Arnold, A. Yang, A. Aguirre, E.T. Harada, D. Korenblum, J. Pollard, A. Bibillo, R. Chen, R. Davis, J.J. Russo, C.W. Fuller, S. Roever, J. Ju, and G.M. Church. “Design and Characterization of A Nanopore-Coupled Polymerase for Single Molecule DNA Sequencing by Synthesis on an Integrated Electronic Array” **The 20th International Conference on Miniaturized Systems for Chemistry and Life Sciences (MicroTAS 2016)** – Dublin, Ireland. October 2016.

S. Kumar, M. Porel, M. Chien, C. Tao, S. Kalachikov, S. Shi, M. Palla, P.B. Stranges, Z. Li, J.J. Russo, G.M. Church, J. Ju. “Polymer Tagged Nucleotides for Single Molecule DNA Sequencing by Synthesis on a Nanopore Array” **The XII International Roundtable on Nucleosides, Nucleotides & Nucleic Acids** – Paris, France. July 2016.

T. Rindzevicius, M.S. Schmidt, K. Wu, A.H. Thilsted, R.K. Lauridsen, T.S. Alstrøm, M. Palla, J. Yang, A. Boisen. “Plasmonic Nanopillar Structures for Surface-Enhanced Raman Scattering Applications” **The 10th Annual TechConnect World Innovation Conference and Expo** – Washington, DC. May 2016.

M. Palla, F.G. Bosco<sup>†</sup>, J. Yang<sup>†</sup>, T. Rindzevicius, T.S. Alstrom, M.S. Schmidt, Q. Lin, A. Boisen, J. Ju. “Mathematical Model for Biomolecular Quantification Using Large-Area Surface-Enhanced Raman Spectroscopy Mapping” **The 14th IEEE Conference on Sensors (IEEE SENSORS 2015)** – Busan, South Korea. November 2015. Selected as top 10% of all conference proceedings.

P.B. Stranges, M. Palla<sup>†</sup>, J. Nivala, C.W. Fuller, S. Kumar, M. Porel, M.-C. Chien, A. Bibillo, M. Dorwart, C. Tao, Z. Li, W. Guo, D. Korenblum, A. Trans, A. Aguirre, E. Liu, T. Harada, J. Pollard, J. Hu, C. Cech, A. Yang, C. Spilman, R. Chen, I. Morozova, S. Kalachikov, S. Shi, J.J. Russo, R. Davis, S. Roever, J. Kasianowicz, J. Ju, G.M. Church. “Single Molecule DNA Sequencing using Electronic

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<sup>†</sup> This author contributed equally to the first author.

Sensory Arrays with Biological Nanopore-bound Polymerase” **National Human Genome Research Institute (NHGRI) Advanced DNA Sequencing Technology Development Meeting** – San Diego, CA. May 2015.

J. Yang, M. Palla<sup>†</sup>, F.G. Bosco<sup>†</sup>, M.S. Schmidt, T. Rindzevicius, A. Boisen, J. Ju, Q. Lin. “A Microfluidic Surface Enhanced Raman Spectroscopic Biosensor Using Aptamer Functionalized Nanopillars” **The 17th International Conference on Solid-State Sensors, Actuators and Microsystems (TRANSDUCERS & EUROSENSORS XXVII)** – Barcelona, Spain. June 2013.

M. Palla, W. Guo, S. Shi, Z. Li, J. Wu, S. Jockusch, C. Guo, J.J. Russo, N.J. Turro, J. Ju. “DNA Sequencing by Synthesis Using Surface-Enhanced Raman Spectroscopy” **244th ACS National Meeting and Exposition** – Philadelphia, PA. August 2012.

J. Zhu, M. Palla, S. Ronca, R. Warpner, J. Ju, Q. Lin. “A MEMS-based Approach to Detection of Single Nucleotide Polymorphisms for Genetic Disorder Diagnosis” **The 25th International Conference on Micro Electro Mechanical Systems (IEEE MEMS 2012)** – Paris, France. February 2012.

J. Zhu, C. Qiu<sup>†</sup>, M. Palla, T. Nguyen, J. Ju, Q. Lin. “A Microfluidic Device for Detection of Single Nucleotide Polymorphisms by Allele Specific Single Base Extension” **The 15th International Conference on Miniaturized Systems for Chemistry and Life Sciences (MicroTAS 2011)** – Seattle, WA. October 2011.

M. Palla, C.-P. Chen, Y. Zhang, J.L. Li, J. Ju, J.-C. Liao. “Mechanism of Flexibility Control for ATP Access of Hepatitis C Virus NS3 Helicase” **Biophysical Society 55th Annual Meeting** – Baltimore, MD. May 2011.

Y. Zhang, M. Palla, J. Li, J.-C. Liao. “Mechanism of Locking Myosin VI Converter in the Unique Pre-Stroke Conformation” **Biophysical Society 55th Annual Meeting** – Baltimore, MD. May 2011.

M. Palla. “Genetomic Promototypes: High-throughput, Computational Design of Synthetic Promoter Regions” **Honors Thesis Presentation**, Clarkson University – Potsdam, NY. May 2007.

## PATENT APPLICATIONS

Church GM, Palla M, Thompson DB, inventors; Harvard College, assignee. Nanopore-based Cas9 Profiling for Genome Engineering. Harvard Docket No. 6685. 2018 January 5.

Ayer A, Church GM, Palla M, Pepin F, Punthambaker S, Stranges PB, inventors; Roche Sequencing Solutions Inc, Roche Diagnostics GmbH, F. Hoffmann-Laroché Ag, Harvard College, assignee. Enzyme screening methods. WIPO Patent Application No. 2019/040546 A1. 2019 February 28.

Church GM, Nivala J, Palla M, Stranges PB, inventors; Harvard College, assignee. Method and system of nanopore-based information encoding. WIPO Patent Application No. 2017/184677. 2017 October 26.

Church GM, Lee H, Palla M, inventors; Harvard College, assignee. Method of making polynucleotides using an anion toroidal vortex. WIPO Patent Application No. 2017/142913 A1. 2017 August 24.

Ju J, Kumar S, Palla M, Russo J, inventors; The Trustees of Columbia University in the City of New York, assignee. Raman cluster tagged molecules for biological imaging. WIPO Patent Application 2014/144883. 2014 September 18.

Lin Q, Boisen A, Yang J, Palla M, Bosco FG, Schmidt MS, Rindzevicius T, Stojanovic MN, Ju J, inventors; The Trustees of Columbia University in the City of New York, assignee. Large-area mapping of uniform SERS-active substrate for reliable, sensitive and specific detection of biomolecules. United States Provisional Application No. 61/813,060. 2013 April 17.

Lin Q, Zhu J, Qiu C, Palla M, Ju J, inventors; The Trustees of Columbia University in the City of New York, assignee. A microfluidic device for detection of single nucleotide polymorphisms by allele specific single base extension. United States Provisional Application No. 61/542,124. 2011 September 30.

## PROJECTS AT COLUMBIA UNIVERSITY

### 1. **Click Chemistry Monitoring** – *Ju Laboratory – Department of Chemical Engineering*

Developed a versatile validation method to monitor copper-free click reaction efficiency for small molecule conjugation. The monitoring principle is based on loss of the Raman signals of alkyne and azido moieties on the partnering molecules caused by non-Raman active triazole formation as a function of time. Since these universal Raman reporter groups are specific for click reactions, this method may facilitate a broad range of applications for monitoring the conjugation efficiency of molecules in diverse areas such as bioconjugation, material science or drug discovery. (July 2013 – December 2013)

### 2. **SERS Nanosensor** – *Ju/Lin/Boisen Laboratory – Department of Chemical/Mechanical Engineering/Micro- and Nanotechnology*

Developed a nanosensor device consisting of aptamer-functionalized metallic nanopillars for sensitive surface enhanced Raman spectroscopy (SERS) quantification of biomolecules. The device utilizes surface plasmon resonance with ultra-high sensitivity properties and provides excellent signal reproducibility and uniformity. The automated collection of large number of vibrational spectra paired with a novel statistical method for quantification provides a framework for the development of a novel, cheap and fast sub-nM biodetection device. (April 2012 – December 2013)

### 3. **Intensity Distribution Model** – *Ju/Lin/Boisen Laboratory – Department of Chemical/Mechanical Engineering/Micro- and Nanotechnology*

Developed an analytical model to predict experimental hotspot intensity distribution on the aptamer functionalized nanopillar substrates for biomolecular quantification. The statistical model may be generally used for biomolecular quantification on any SERS substrates with planar geometries, in which the hotspots can be approximated as the electromagnetic enhancement fields generated by closely spaced dimers. The potential for single molecule detection was also shown by estimating the number of vasopressin molecules probed by SERS during biomolecular quantification, thus opening up an exciting new chapter in the field of SERS quantification. (April 2012 – December 2013)

### 4. **Raman Sequencing** – *Ju/Turro Laboratory – Department of Chemical Engineering*

Developed a third-generation sequencing technology combining novel synthetic biochemistry with plasmonic nanostructures of sub-wavelength dimensions. Surface enhanced Raman scattering (SERS) active substrates coupled with innovative Raman tag selection in DNA sequencing are highly desirable and will open the door to routine, reliable, and continuous high-throughput, personalized genome analysis possibly coupled with microfluidic technology. (July 2011 – December 2013)

### 5. **Microfluidic Genotyping** – *Ju/Lin Laboratory – Department of Chemical/Mechanical Engineering*

Developed a microfluidic device for genotyping based on the single-base extension and solid-phase capture methods previously developed in our lab. The device reduces processing time and allows for

rapid analysis by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). In addition, it allows simultaneous processing of multiple samples and can be reused after regeneration of beads with no carryover effects. These results indicate that the microfluidic device is a low-cost tool that enhances sample cleanup prior to MS for single nucleotide polymorphism (SNP) genotyping. (March 2010 – December 2013)

#### **6. Molecular Dynamics Simulation – Liao Laboratory – Department of Mechanical Engineering**

Investigated the behavior of the ATP active site of hepatitis C virus (HCV) NS3 helicase during polynucleotide unwinding. Used molecular dynamics (MD) simulation to examine the mutational effect of T324, a hinge residue connecting domains 1 and 2, on the dynamics of the ATP binding site. Found that the ATP binding cleft flexibility is controlled by a long-range atomic network, affecting residues located in domain 1. These results call for future evaluation to elucidate the exact relationship between ATPase activity decrease and 3D structural changes, and fuel new therapeutic development of HCV. (February 2010 – November 2011)

#### **7. Walkameter – Ju Laboratory – Department of Chemical Engineering**

Designed and tested a microfluidic automation system composed of: PDMS chamber, temperature and fluidics control sub-units. Implemented a modular LINUX software for fluidic and temperature control in Python. Demonstrated the feasibility of a novel biochemistry technique to extend the read-length of human DNA sequencing on a high-throughput manner, and its applicability to serve as a supplementary biochemistry step for current next-generation sequencing instruments. (September 2008 – February 2010)

### **OTHER RESEARCH EXPERIENCE**

#### **Harvard Medical School, Department of Genetics – Church Laboratory – Boston, MA**

Employed as a R&D Engineer to develop a next-generation, cost-effective, open-source DNA sequencing instrument (“Polonator”) in the Church Lab. Conducted, both independently and in a team environment, optical and heat transfer experiments to optimize the fluidics subsystem of the biomedical device. Gained theoretical knowledge and practical experience in mechanical, electrical, computer and biological engineering. Learned fundamental principles of genomic DNA preparation, amplification and analysis, as well as automated sequencing data generation/storage. (August 2007 – September 2008)

#### **Honors Program, Clarkson University – Potsdam, NY**

Honors Thesis: “Genetomic Promototypes: High-throughput, Computational Design of Synthetic Promoter Regions”. Implemented a user-friendly, advanced software package called BASHER for the high-throughput design of synthetic promoter regions of *Saccharomyces cerevisiae*. Built a powerful and flexible tool for hypothesis testing of regulatory logic in the eukaryotic yeast cell. Beside site-directed mutagenesis, structural analysis and investigation of transcription regulation, incorporated combinational and spatial effects of *cis*-binding sites into the package. (September – May 2007)

#### **Harvard Medical School, Department of Genetics – Church Laboratory – Boston, MA**

Conducted research in the Church Lab with an interdisciplinary group of experimental and computational biologists focusing on the development of a wide range of new technologies in the field of genomics / systems biology. Developed interactive software for genomic promoter sequence design. Analyzed unique, large-scale genomic datasets using state of the art bioinformatics tools, and developed novel algorithms and software tools. Gained strong computer programming skills in Perl and MATLAB. (May – August 2005, January – August 2006)

### **SUNY Research Foundation, SUNY Potsdam – Potsdam, NY**

Participated in faculty-undergraduate summer research program designing a computer simulation of the transmission of DNA through multiple generations of isolated populations. Investigated the Hardy-Weinberg Principle through the statistical analysis of the ratio of recessive to dominant genes within a population. Modeled the reproduction and growth of populations with mating behavior and genetic composition according to Mendelian genetic principles. Work involved population genetics, probabilistic computational biology, statistical analysis, software development, theory of random walks, complexity theory. (May – August 2004)

### **State University of New York College at Potsdam – Potsdam, NY**

Explored bioinformatics and computer aided drug design through the Presidential Scholar Program, which provides recognition and additional financial resources for independent research projects. Visited universities and pharmaceutical research laboratories targeting genomics development. Attended bioinformatics workshops at the Ninth Annual Consortium for Computing Sciences Northeastern Conference at Union College. (August 2004 – January 2005)

## **PROJECT MANAGEMENT**

### **Harvard Medical School, Department of Genetics – Church Laboratory – Boston, MA**

Lead an industrial-academic research collaboration related to the development of an electrode array based single molecule DNA sequencing platform (Genia Technologies, Inc). In a small team setting, integrated fundamental research innovations, such as novel protein design, measurement and analysis techniques, into the partner's corporate objectives for technology advancement. Negotiated and drafted professional contracts on intellectual property (IP), confidentiality and publication procedures with in-house lawyers. Lead weekly collaborative teleconferences to ensure progress in the project and communicated about alignment with joint and individual objectives. On an annual basis, participated in the company's scientific training workshops to learn about the latest technical innovations and gain hands-on experience on laboratory/instrumentation protocols. Co-written NIH grant proposals and updates with industry partner. Published results in scientific papers of highly ranked peer-reviewed journals (PNAS). Generated IP (US patent application) for large-scale de novo gene synthesis with the utilization of the nanopore-array platform. (May 2014 – present)

### **Wyss Institute of Biologically Inspired Engineering, Synthetic Biology Platform – Boston, MA**

Worked on the development of a next-generation sequencing technique to resolve haplotype polymorphisms by the integration of super-resolution microscopy, DNA stretching and structural ligation of DNA origami barcodes. Demonstrated successful nick translation with fluorescently labeled nucleotides and DNA polymerase I on surface-immobilized, stretched DNA molecules. Verified correct digestion spacing and proved the feasibility of spatial ligation by using fluorescently labeled, nick-site specific probes targeting the arrayed DNA. Finally, developed an image analysis pipeline to obtain coordinates of fluorescent labels on stretched single DNA molecules. (May 2014 – December 2014)

## **TECHNICAL SKILLS**

- **Genomics:** primer design, PCR, DNA purification, SNP detection/analysis, DNA sequencing by synthesis, Illumina Genome Analyzer, MALDI-TOF MS, Raman/SERS spectroscopy
- **Bioinformatics:** genomic data analysis, base-calling algorithms, multiple-sequence alignment, ion current signal processing, DNA barcode generation algorithms, signal classifiers, principal component analysis

- Computer Languages: Python, Perl, C/C++, MATLAB, R, Java, Scheme
- Operating Systems: Microsoft Windows, Linux, Mac OS
- Software Experience: Pro/ENGINEER, Fluent, LabVIEW, Gromacs, VMD, Simulink, Maple
- Engineering lab knowledge: sampling statistics, uncertainty analysis, error propagation, DAQ
- Chemistry lab knowledge: titration- and filtration techniques; spectral- and qualitative analysis
- Technical writing and presentations
- **Languages:** English (fluent), German (intermediate), Hungarian (native)

## PRESS COVERAGE

Think. Make. Matter. Join our Tech Xperience Week. (October 21, 2018). Retrieved from <https://brainporteindhoven.com/tech-xperience/>

Meet the Candidates. These are the stories of the men and women of the Tech Xperience Week. (October 28, 2018). Retrieved from <https://brainporteindhoven.com/candidates/mirko-palla/>

Kriz, Alan (September 19, 2017). [“Beyond Bayer Walls: A Novel Approach to Problem-Solving”](#) (Blog post). Bayer Crop Science. Retrieved December 20, 2018.

Cooper, Leigh (November 1, 2016). [“Improving DNA sequencing”](#). Washington, DC: **In This Issue**, PNAS. Retrieved November 7, 2016.

Johnson, Dexter (October 13, 2016). [“Personalized Medicine Draws Closer With Cheap and Accurate DNA Sequencer”](#) (Press release). New York, NY: **IEEE Spectrum**. Retrieved November 7, 2016.

Boettner, Benjamin (October 11, 2016). [“Poring over DNA”](#) (Press release). Washington, DC: **EurekAlert!**/American Association for the Advancement of Science (AAAS). Retrieved November 7, 2016.

[“Advancing nanopore sensing towards lower cost and more accurate DNA sequencing”](#) (Press release). Honolulu, HI: **Nanowerk**. October 10, 2016. Retrieved November 7, 2016.

## ATHLETIC ACTIVITIES

- |                                      |   |
|--------------------------------------|---|
| <b>2014-2019</b>                     | <b>Harvard University Med/Law Hockey Team</b><br>Competed in the Larz Anderson Adult Men's Hockey League – Brookline, MA                          |
| <b>2008-2014</b>                     | <b>Columbia University Men's Hockey Team</b><br>Competed in the American Collegiate Hockey Association (AMCA) – New York, NY                      |
| <b>2007-2008</b><br><b>2004-2007</b> | Competed in the New England Senior Hockey League (NESHSL) – Boston, MA<br>Member of the Clarkson University Men's Club Hockey Team – Potsdam, NY  |
| <b>2002-2004</b>                     | <b>Potsdam State Men's Hockey Team</b><br>Competed in the SUNYAC university hockey league (NCAA Division III) – Potsdam, NY                       |
| <b>2001-2002</b>                     | <b>Lanark Thunder Junior Hockey Club</b><br>Competed in the Central Junior A Junior Hockey League – Ottawa, ON Canada                             |
| <b>2000-2001</b>                     | <b>Hungarian National Junior U-20 Ice Hockey Team</b><br>Finished 7th place at the IIHF World Junior U-20 Championship Div II – Kaunas, Lithuania |

**Athens Aeros Junior Hockey Club**

Competed in the Eastern Ontario Junior Hockey League – Ottawa, ON Canada  
All-star selection for the Rideau Division

**1999-2000****Hungarian National Junior U-20 Ice Hockey Team**

Finished 4th place at the IIHF World Junior U-20 Championship Pool C – Nagano, Japan

**Hungarian National In-line Hockey Team**

Finished 11th place at the IIHF In-line Hockey World Cup – Prague, Czech Republic  
Qualified to the 2000-2001 IIHF In-line Hockey World Championship

**Dunnville Terriers Junior Hockey Club**

Competed in the Niagara District Junior Hockey League – Welland, ON Canada

**1998-1999****Hungarian National Junior U-18 Ice Hockey Team**

Finished 7th at the IIHF World Junior U-18 Championship Pool B – Pralognan, France  
Assistant captain of the national team  
MVP of the game against Italy

Competed in the Niagara District Junior Hockey League – Welland, ON Canada

**VOLUNTEERING****Tree Planting Crew**

Newton Tree Conservancy – Community Tree Plantings – Newton, MA

- In a small group setting, planted ~20 bare-root trees in the neighborhood. Helped with digging, stone removal, filling watering bags, spreading mulch and cleanup during the 3-hour planting process. (04/29/2017)

**Package Sorting Volunteer**

Cradles to Crayons – Community Outreach – Boston, MA

- At the Giving Factory warehouse, worked in a team of 20 people to inspect, sort and package new and like-new donations into customized children's packages. (03/25/2017)

**Food Pantry Volunteer**

American Red Cross of Massachusetts – Poverty Alleviation – Roxbury, MA

- Provided a 5-day emergency supply of food to low-income community members. In a team environment, sorted/packaged food items, then distributed them to clients, and helped carry bags out of the pantry for clients to their cars. (April 2016)

**Hurricane Sandy Recovery Crew**

New York Cares – Disaster Relief – New York, NY

- Participated in the cleanup of the Happy Warrior Playground on West 98th Street and Amsterdam Avenue. Removed fallen tree branches and other debris; raked and disposed leaves. (11/02/2012)
- Carried out sorting and packaging of blankets, clothes, food and cleaning supplies to be shipped to the affected areas at the Riverside Church. (11/12/2012)
- Under the leadership of the Columbia Graduate Council, assisted Threads non-profit organization to clean homes from debris, damaged furniture and destroyed household items. (11/15/2012)