# BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person.

**DO NOT EXCEED FIVE PAGES.**

**NAME**: Bojana Gligorijevic

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

**POSITION TITLE**: Associate Professor

**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.)*

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| --- | --- | --- | --- |
| INSTITUTION AND LOCATION | DEGREE  *(if applicable)* | Completion Date  MM/YYYY | FIELD OF STUDY |
| Belgrade University, Belgrade, Serbia | BS | 2001 | Analytical Chemistry |
| Georgetown University, Washington, D.C. | MS | 2002-‘05 | Chemistry/ Biophysics |
| Georgetown University, Washington, D.C. | PhD | 2005-‘07 | Biophysics/Microscopy |
| Albert Einstein College of Medicine, New York  Albert Einstein College of Medicine, New York | Postdoc  Instructor | 2007-‘12  2012-‘15 | Tumor Microenvironment Microscopy  Microscopy Applications of  Machine Learning |

# A. Personal Statement

My lab investigates the dynamics of cancer cell metastasis, with a focus on invadopodia, ECM-degrading protrusions on the cancer cell membrane. To address intrinsic and extrinsic, microenvironment-driven mechanisms of metastasis, my lab uses established and develops new intravital microscopy technologies. We integrate microscopy, image processing & machine learning with cancer biology, microfabrication and mathematical models. In particular, by developing the first longitudinal imaging window in mice, and combining it with photoconvertible fluorescent proteins, we were able to demonstrate itineraries of individual cancer cells from the primary tumor, through the blood vessels and inside the lung (*Nature Methods, Nature Protocols*). Next, by using intravital multiphoton microscopy and support vector machine classification, we were the first to demonstrate invadopodia assembly is a necessary step for blood vessel entry (*Plos Bio*). Most recently, using time-lapse of FUCCI-labeled tumors, spheroids and cells in confinement, we demonstrated that during G1 phase of the cell cycle, the cancer cells move at high velocities (*APL Bioengineering*) and assemble invadopodia, which is controlled via cytoplasmic pool of p27 and its interaction with Tks5 and cortactin in invadopodia (*J Cell Science*).

My laboratory offers the opportunity to train in developing and implementation of cancer imaging techniques and cancer mechanobiology. Mentees are exposed to a diverse set of microscopy-centric approaches applied to cancer, both *in vitro* and *in vivo*. My teaching and service at Temple are devoted to implementing microscopy towards solving biomedical questions. As a Director of Light Microscopy shared resources at Temple Engineering, me and my mentees have trained >100 students and collaborated with >20 labs on their microscopy applications. In addition, I have developed a hands-on course on Biophotonics for students of Bioengineering. This course has evolved as a result of my long experience of teaching microscopy, which includes MBL course in Woods Hole, as well as teaching microscopy to PhD and medical students at Albert Einstein College of Medicine. On international level, I have so far contributed a number of chapters in microscopy books; I am an active member of BINA Imaging Network and currently on organizing committee of Intravital Imaging of Cancer seminars, together with peers from France and Australia. I am excited to extend my collaborations, training and mentoring to FCCC as a Co-Director of BIF and have now established a satellite office and lab there for this purpose.

1. B. Gligorijevic\*, D. Kedrin\*, J. Wyckoff, V.V.Verkhusha, J. Condeelis, J. E. Segall, J. van Rheenen,”Intravital imaging of metastatic cell behavior through an orthotopic Mammary Imaging Window” **Nature** [**Methods**(2008),5:1019-1021 PMCID:](http://news.bbc.co.uk/2/hi/health/7711650.stm) PMC2820719
2. B. Gligorijevic, A. Bergman, J. Condeelis: ”Multiparametric Classification Links Tumor Microenvironments with Tumor Cell Phenotype”, **Plos Biology** (2014) 12: 1-15, e1001995. PMCID: PMC4227649
3. B. Bayarmagnai, L. Perrin, K. Esmaeili, X. Graña, E. Tüzel, B. Gligorijevic.“Invadopodia-mediated degradation is enriched in the G1 phase of the cell cycle”, **Journal of Cell Science** (2019) doi: 10.1242/jcs.227116.
4. L. Perrin, T. Tucker, B. Gligorijevic, “Time-Resolved Fluorescence Imaging and Analysis of Cancer Cell Invasion in the 3D Spheroid Model”, Preclinical models and imaging modalities of tumor microenvironment in metastasis, **Jove** (2021), doi 10.3791/61902

# B. Positions and Honors

**Positions**

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| --- | --- |
| 1998-2000 | Undergraduate researcher, University of Belgrade, Department of [Chemistry](http://www.chem.bg.ac.yu/index-en.html) |
| 1999 | Research Assistant, Federal Bureau for Measurements and Precious Metals, Laboratory for Ionizing Radiation (Belgrade, Serbia) |
| 2001-2002 | Research Talent, University of Belgrade, Faculty of Technology, Department of Environmental Engineering |
| 2000-2002 | Research Talent, [Military Medical Academy,](http://www.vma.mod.gov.yu/VMA_MMA/En/Vma_E_Index.htm) Poison Control Center, Laboratory of Toxicology Research |
| 2002-2007 | PhD student, [Georgetown University, Department of Chemistry](http://www8.georgetown.edu/departments/chemistry/) |
| 2007-2012 | Post-doctoral fellow, Albert Einstein College of Medicine, Department of Anatomy & Structural Biology, Program in Microenvironment and Metastasis, Gruss-Lipper Biophotonic Center. |
| 2012-2015 | Research Faculty, Albert Einstein College of Medicine, Systems and Computational Biology Department |
| 03/01/2015-07/01/2020 | Assistant Professor, Bioengineering Department, Temple University |
| 09/01/2015-current | Primary Member, Cancer Signaling & Epigenetics, Fox Chase Cancer Center |
| 05/28/2020-current | Director of Light Microscopy, Bioengineering Department, Temple University |
| 07/01/2020-current | Associate Professor, Bioengineering Department, Temple University |
| 01/01/2021-current | Co-Director of Biological Imaging Light Facility, Fox Chase Cancer Center |

**Honors**

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| --- | --- |
| 2001-2002 | Research Fellowship, University of Belgrade |
| 2000-2002 | Research Talent Fellowship, Military Medical Academy, Belgrade, Serbia |
| 2002 | Espenscheid PhD Fellowship (top 2%), Georgetown University |
| 2007 | Concept Award, Department of Defense Breast Cancer Research Program |
| 2008 | 5th Annual Belfer Prize for Outstanding Postdoctoral Research (top 3%) |
| 2008 | American Society of Cell Biology, “Newsworthy” talk (top 1%, 12/1,229) |
| 2008 | Featured in Nature Milestones: Light Microscopy, In situ and in vivo microscopy |
| 2010 | Charles Revson Foundation Biomedical Research Fellowship (8-10 annually) |
| 2010 | Dennis Shields Postdoctoral Research Prize (3 awarded annually) |
| 2013 | K99 Pathway to Independence Award NIH/NCI |
| 2014 | K22 Career Transition Award (passed due to K99) |
| 2014 | ATIP Avenir European Young Group Leader- passed for Temple Bioengineering |
| 2016 | Concern Foundation “Conquer Cancer Now” Young Faculty Award (~10 annually) |
| 2020 | American Cancer Foundation “Research Scholar” Award |
| 2015,16,17,18,19,20 | Temple University Faculty Merit Awards for Exceptional Research and Service |

04/2021 Fellow-Invited seminar, Pediatric Oncology Branch, NCI (1 annually)

**Professional affiliations**

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| --- | --- |
| Journals  Conferences/  workshops  Ad Hoc Reviews | * Editorial Board Member, Frontiers in Cell & Developmental Biology * Editorial Board Member, Cancer Biology & Therapy   + 2019, 2020, 2021-Scientific Co-chair, ASCB-EMBO Subgroup: Cell-Matrix and Cell-Cell Interactions in 3D Environments * 2021-Organizing Co-Chair, Intravital Imaging of Tumor Progression, Global Seminars (Chairs from Australia, USA and Europe) * 2021-European Society for Molecular Imaging (ESMI) meeting judge * 2019-Program Chair and Co-organizer, Philly Motility Biannual Symposium * 2015-Organizing Vice Chair, Integrative Mechano-Chemical Signaling in Invasion, Nice, France * 2010-Tumor Microenvironment Network NCI- Junior Investigator Committee * 2020-Faculty, Woods Hole Optical Imaging Course * NIH, NCI Special Emphasis Panel ZCA1 SRB-X (O1) R, U54   Cellular Cancer Biology Imaging Research Centers (CCBIR)   * NIH, NIDDK, Diabetes, Endocrinology & Metabolic Diseases-B * ongoing, NIH, National Cancer Institute, Tumor Progression and metastasis section * ongoing, Department of Defense, Pathobiology sections, Breast Cancer Research Program * American Cancer Society, Cancer Structure and Metastasis Study section * National Science Foundation, Systems and Molecular Biology, GRF program * AACR INNOVATOR Award in Tumor Microenvironment, Landon Foundation * National Science Foundation, ARI- R2, Chemistry study section |
| Expert Grant Reviews | * Portuguese FCT- Fundacao para a Sciencia e a Tecnologia * Wellcome Trust, Dept Biotechnology, India Alliance |
|  | * Breast Cancer Now foundation, United Kingdom |
|  | * The Science Fund of the Republic of Serbia |
|  | * Estonian Research Council (ETIS) * National Science Foundation of Poland * Swiss National Science Foundation * PA Breast Cancer Coalition (PABCC) |

**Ad hoc reviews:** Nature Nanotechnology, Nature Protocols, Nature Scientific Reports, PNAS, Science Advances, Cancer Research, Cancer Reports, Journal of Cell Biology, European J. of Cell Biology, Integrative Biology, Disease Models & Mechanisms, Plos Biology, Plos One, Bioinformatics, APL Bioengineering, Frontiers in Cell and Developmental Biology, Acta Biomaterialia, Cell Adhesion and Migration, Experimental Cell Research, Journal of Visual Experiments, Methods, Molecules, Oncogene, Cells, Biophysical Journal.

**Professional Memberships:** American Society for Cell Biology, Biophysical Society, Invadosome Consortium, SigmaXi society, Metastasis Research Society, American Society for Matrix Biology

### C. Contribution to Science

I. The genetic basis of resistance in malaria is very similar to stomach cancers, involving (pf)mdr1 and (pf)crt. Due to the lack of suitable technology, opposing theories on mechanisms of resistance were never tested. Led by this need, I have initiated collaboration with physicists, customized a spinning disk microscope and developed several malaria live imaging technologies. This allowed me to quantitatively show chloroquine mechanism of action is based on the inhibition of heme dimerization and test its stage-specificity. My two first-authored manuscriptsin Biochemistry were covered in Editor letter in Biophotonic International and the SYBR Green assay we have developed is now used as the official malarial drug test at Walter Reed Institute.

* 1. B. Gligorijevic, T. N. Bennett, R. McAllister, J. S. Urbach and P. D. Roepe, ["Spinning Disk Confocal](http://pubs.acs.org/cgi-bin/sample.cgi/bichaw/2006/45/i41/html/bi0610348.html) [Microscopy of Live, Intraerythrocytic Malarial Parasites. 2. Altered Vacuolar Volume Regulation in Drug Resistant Malaria",](http://pubs.acs.org/cgi-bin/sample.cgi/bichaw/2006/45/i41/html/bi0610348.html) **Biochemistry** (2006), 45(42):12411 – 12423. (“Hot Article of Biochemistry”, 11/2006) PMCID: PMC400551

1. B. Gligorijevic, R. McAllister, J. Urbach and P. D. Roepe, ["Spinning Disc Confocal Microscopy of malaria 1.Quantification of Hemozoin Development for Drug Sensitive versus Resistant Malaria",](http://pubs.acs.org/cgi-bin/sample.cgi/bichaw/2006/45/i41/html/bi061033f.html) **Biochemistry** (2006), 45(42):12400 - 12410 PMID: 17029396
2. B. Gligorijevic, K. Purdy, D. A. Elliott, R. A. Cooper and P. D. Roepe "Stage independent chloroquine resistance and chloroquine toxicity revealed via Spinning Disc Confocal Microscopy" **Molecular Biochemical Parasitology** (2008), 159(1):7-23 PMCID: PMC2440633
3. T. N. Bennett, M. Paguio, B. Gligorijevic, C. Sidieu, A. D. Kosar, E. Davidson, P. D. Roepe ["Novel, Rapid and Inexpensive Cell- Based Quantitation of Antimalarial Drug Efficacy"](http://aac.asm.org/cgi/content/full/48/5/1807) **Antimicrobial Agents and Chemotherapy**(2004), 48(5):1807-1810.

II. I advanced intravital multiphoton microscopy to study perivascular niche in tumor models, in living animals. I developed methodologies to simultaneously visualize several components of tumor microenvironment through time, at subcellular resolution; to be able to manipulate cell motility in primary tumor and finally, to monitor cell motility *in vivo* over days. This task demanded the collaborations with chemists developing fluorescent proteins, engineers constructing microfluidics and immunologists studying host-cell behavior. It resulted in high profile study in *Nature Methods* (cited >200 times/7 years), featured in *Nature Milestones in Light Microscopy* collection.

1. B. Gligorijevic\*, D. Kedrin\*, J. Wyckoff, V.V.Verkhusha, J. Condeelis, J. E. Segall, J. van Rheenen, “Intravital imaging of metastatic cell behavior through an orthotopic Mammary Imaging Window” **Nature** [**Methods**(2008),5:1019-1021 PMCID:](http://news.bbc.co.uk/2/hi/health/7711650.stm) PMC2820719
2. B. Gligorijevic\*, W. K. Raja\*, J. Wyckoff, J. Condeelis, J.Castracane, “A new chemotaxis device for cell migration studies”, **Integrative Biology** (2010), 2:696-706 PMCID: PMC4026270
3. D. Entenberg, J. Wyckoff, B. Gligorijevic, E. T. Roussos, V.V.Verkhusha, J.Pollard, J. Condeelis “Setup and use of a two-laser multiphoton microscope for multichannel intravital fluorescence imaging”, **Nature Protocols** (2011),6:1500–1520, PMCID: PMC4028841
4. L. Perrin, B. Bayarmagnai, B. Gligorijevic, “Frontiers in intravital multiphoton microscopy of cancer”, **Cancer Reports** (2019), e1192. <https://doi.org/10.1002/cnr2.1192>
5. Using my unique approaches, I was able to demonstrate that ECM-remodeling protrusions in cancer cells (“invadopodia”) are necessary for intravasation and metastasis *in vivo*, and that they can be inhibited via microenvironment modulation. This work solved a 30-year-long controversy on invadopodia relevance for metastasis and microenvironmental cues which lead to assembly. Prior literature has mainly investigated invadopodia formation on cancer cells plated on dishes coated with extracellular matrix proteins. Under controlled conditions of the 2D culture, cells spread and invadopodia appear as small (1 µm) punctate enrichments of actin surrounding nucleus and create holes in the matrix. In the heterogeneous, dynamic, 3D tissue conditions it was necessary to establish new tools for identification and analysis of invadopodia (topographical, morphological, structural and functional). This work suggested that invadopodia may be a good predictor of metastasis and clinical target.
6. B. Gligorijevic\*, J. Wyckoff\*, H. Yamaguchi, Y. Wang, J. Condeelis: “N-WASP-mediated invadopodium formation is involved in intravasation and lung metastasis of mammary tumors”, **Journal of Cell Science** (2012), 125:724-734 PMCID: PMC3367832
7. E. T. Roussos, M. Balsamo, S. K. Alford, J. B. Wyckoff, B. Gligorijevic, Y. Wang, M. Pozzuto, R.Stobezki, S. Goswami, D. A. Lauffenburger, A.R. Bresnick,F. B. Gertler and J. S. Condeelis, “Mena invasive promotes multicellular streaming motility and transendothelial migration in a mouse model of breast cancer”*,* **Journal of Cell Science**(2011), 124:2120-2132 PMCID: PMC3113666
8. E. Genot, B. Gligorijevic, “Invadosomes in their natural habitat”, **European Journal of Cell Biology** (2014), PMCID: [PMC4262535](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4262535/)
9. F. Tonisen, L. Perrin. K, van der Dries, A. Cambi, B. Gligorijevic, “EP4 receptor role in invasion of breast carcinoma” **European Journal of Cell Biology** (2017) PMCID: [PMC5362301](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5362301/)
10. In summary, my work on intravital imaging tools transformed the cancer biology field in two distinct manners: First, by developing the first method for repeated, quantitative imaging of the same cell populations in living animals, we allowed researchers to view metastasis directly and study individual steps. The project resulted in a *Nature Methods* publication cited almost 300 times since 2009 (Google Scholar), followed by several studies which used this technology to tackle molecular mechanisms in metastasis, each with > 100 citations. Second, I demonstrated that ECM-remodeling protrusions in cancer cells (“*invadopodia*”) are necessary for cancer cell intravasation and metastasis *in vivo*, and that they can be inhibited via microenvironment modulation. During my K99 period, I worked on integration of intravital imaging with systems view. I have proposed the workflow to follow (see a. and b.) towards statistical classification of cell motility phenotypes in cancer model as a context-based decision. My experimental work has soon demonstrated this approach as predictive (see a.) and influenced both mathematical and cancer biologists' view on cell plasticity.
11. B. Gligorijevic, A. Bergman, J. Condeelis: “Multiparametric Classification Links Tumor Microenvironments with Tumor Cell Phenotype”, **Plos Biology** (2014) 12: 1-15, e1001995. PMCID: PMC4227649
12. Bergman, J. Condeelis, B. Gligorijevic, “Invadopodia in Context”, **Cell Adhesion and Migration** (2014) 8:273-279. PMCID: 4198352
13. Bergman, B. Gligorijevic: “Niche Construction Game Cancer Cells Play”, in Physics of Cancer collection, **European Physics Journal Plus** (2015) 130:203 PMCID: [PMC5027994](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5027994/)
14. B. Bayarmagnai, L. Perrin., K. Esmaeili, B. Gligorijevic: “Intravital imaging of cell migration”, **Methods in molecular biology** (2018), 1749:175-193. PMCID: PMC5996994.
15. My lab is currently devoted to paving a path to integration of biophotonics and systems view towards revealing mechanisms of cell decision-making in cancer and metastasis. With recent technological advances, we have the opportunity to combine the 4D in vivo/in vitro microscopy and computational/mathematical models into Systems Microscopy. Integrative approach to studying the tissue microenvironment and niches within incorporates and extend reductionist findings, giving rise to hypotheses at a system level.
16. K. Esmaeili, A. Bergman, B. Gligorijevic “Extracellular matrix cross-linking regulates invadopodia dynamics.” **Biophysical Journal** (2018), 114:1455-1466. PMCID: PMC5883616
17. K. Esmaeili, E. Cardenas De La Hoz, AR. Cohen, B. Gligorijevic “Contact guidance is cell cycle dependent" **APL Bioengineering** (2018), 2(3):031904. PMCID: PMC5997297.
18. Bayarmagnai B., Perrin L., Esmaeili K., Graña X., Tüzel E., Gligorijevic B. **“**Invadopodia-mediated degradation is enriched in the G1 phase of the cell cycle”, **Journal of Cell Science** (2019) doi: 10.1242/jcs.227116.
19. L. Perrin, B. Bayarmagnai, E. Tüzel and B. Gligorijevic, "Invadopodia enable cooperative invasion and metastasis of breast cancer cells", **BioRxiv** (2021) doi: https://doi.org/10.1101/2021.02.13.431047

**My Bibliography:** <https://www.ncbi.nlm.nih.gov/pubmed/?term=gligorijevic+bojana>

**D. Research Support**

## Ongoing Research Support

NIH R01 CA230777 Gligorijevic (PI) 04/18/2019-03/31/2024

Targeting invadopodia-related mechanisms of cancer cell invasion and metastasis

Role: PI

ACS Research Scholar Grant Gligorijevic (PI) 09/01/2020-08/31/2024

Coordination of Cell Cycle and Invasion in Tumor Microenvironment Context

Role: PI

NIH 3P30CA006927-55S4, Fisher (PI)  07/01/1997-07/31/2021

Comprehensive Cancer Center Program at Fox Chase

Role: Co-Director

NIH 1U54CA221704 / 1U54CA221705, Ma (PI)  09/19/2018-08/31/2023

The Synergistic Partnership for Enhancing Equity in Cancer Health

Role: Collaborator

## Completed Research Support (last 3 years)

K99/R00 5CA172360 Gligorijevic (PI) 08/07/2013-07/31/2019

Systems microscopy of tumor cell motility in microenvironment context.

Role: PI

Conquer Cancer Now, Concern Foundation, Gligorijevic (PI) 07/01/2016-06/31/2018

Real-Time Intravital Imaging of Cancer Cell Cycle and Motility States

Role: PI