CURRICULUM VITAE

Artem K. Efremov (Yefremov)

Postdoctoral Research Fellow,

Mechanobiology Institute, National University of Singapore

5A Engineering Drive 1, Singapore, 117411

E-mail: mbiay@nus.edu.sg

Personal web-site: www.artem-efremov.org

Phone: +658348-5500 (mobile)

Research interests

- Single-molecule kinetics, thermodynamics and force-spectroscopy methods.
- Intracellular transport and molecular motors.
- Cytoskeletal dynamics and cellular mechanobiology.
- DNA-architectural proteins.

Education

- **Undergraduate study**, Moscow State University, Physics Faculty, Department of Biophysics, Moscow, Russia, 09/1998–01/2004.
- **M.Sc.** degree with honor (Master of Science's degree in physics, specialization: biochemical physics). Title of the thesis: "Mechanical model of microtubule", 01/2004.
- **Graduate study**, Moscow State University, Physics Faculty, Department of Biophysics; and National Research Centre for Hematology, Russian Academy of Medical Sciences, Moscow, Russia, 05/2004–07/2008.
- **Ph.D.** degree (Ph.D. in physics, specialization: biophysics). Title of the thesis: "Study of microtubules interaction with chromosome kinetochores", 07/2008.

Honors, Awards, Fellowships

- 2003-2004 – Vernov Scholarship, Moscow State University.
- 2003-2004 – Moscow Scholarship, Moscow State University.

- 2004 – Intel award for the second-best student science work at conference “Numerical geometry, grid generation and scientific computing”, A.A. Dorodnicyn Computer Center, Russian Academy of Sciences, Moscow, Russia, 28th June – 1st July, 2004.
- 2005 – Winner of graduate student competition “Moscow Grants 2005” in the nomination “Biology” (from Moscow Government and International Soros Science Education Program).
- 2008 – American Society for Cell Biology, Cell Dance 2008 video contest, 2nd place.

Teaching/mentoring experience

- 2016-2018 – co-lecturer of Advanced Biophysics course (PC5213) for Master and PhD degree students, Faculty of Science, National University of Singapore. I have been teaching a lecture course, which I have prepared by myself, that describes the major experimental and theoretical biophysical methods widely used in modern single-molecule studies to Master and PhD students starting from early 2016. The course has got many positive feedbacks from students and achieved one of the highest scores among the teaching modules of level 5 (highest university level) taught to Master and PhD students in National University of Singapore, Physics Department.
- 2018 – currently I am supervising a computational / theoretical project aimed at establishing an online server that would allow visitors of the laboratory web-site to run highly advanced transfer-matrix calculations in order to predict the structure and conformation of DNA interacting with DNA-binding proteins under force and torque constraints applied to the DNA. Supervised research group working on this project involves one PhD student (Ladislav Hovan) and one Research Assistant (Yang Kaiyuan). Current version of the on-line program can be found via the following web-link:

  https://www.physics.nus.edu.sg/~biosmm/yjv2_Calculator.html
- Number of currently and previously co-supervised graduate students: 6.

Research experience

- **Undergraduate research assistant**, Moscow State University, 2001-2004.
  PI: Prof. Fazly I. Ataullakhanov, D.Sc.
  Project title: mathematical modeling of microtubule dynamics.
- **Graduate research assistant**, University of Colorado at Boulder, Moscow State University and National Research Center for Hematology, Russian Academy of Medical Sciences, 2004-2008.
  PIs: Prof. Fazly I. Ataullakhanov, D.Sc. and Prof. Richard J. McIntosh.
  Project title: investigation of kinetochore-microtubule interactions in higher and lower eukaryotes.
- **Postdoctoral research fellow**, National University of Singapore and Singapore-MIT Alliance for Research and Technology (S.M.A.R.T.), 2009-2011.
  PI: Assoc. Prof. Zhisong Wang and Prof. Jianshu Cao.
  Project title 1: studying of general physical principles underlying the molecular motors' working mechanism.
  Project title 2: investigation of the cytoadhesion properties of malaria infected red blood cells in shear flow.
- **Postdoctoral research fellow**, Rice University, 2011-2013.
  PI: Assoc. Prof. Michael R. Diehl.

Project title: studying of molecular motors cooperation in intracellular transportation.

- **Senior postdoctoral research fellow**, Mechanobiology Institute, National University of Singapore, 2013-present.
  PI: Prof. Jie Yan.
  Project title 1: application of force-spectroscopy methods for investigation of DNA-binding properties of architectural proteins, and exploration of DNA-protein interactions under applied mechanical constraints.
  Project title 2: role of myosin II motor proteins and formins in filopodia dynamics (independent research in collaboration with Prof. Alexander Bershadsky lab).

Publication list

1. M.I. Molodtsov, E.L. Grishchuk, **A.K. Efremov**, J.R. McIntosh, F.I. Ataullakhanov. 2005. Force production by depolymerizing microtubules: a theoretical study. *Proc. Natl. Acad. Sci. USA*, 102:4353-8.

   [*F1000 recommendation*]

   Web-link: http://www.pnas.org/content/102/12/4353

2. **Artem Efremov**, Ekaterina L. Grishchuk, J. Richard McIntosh,Fazly I. Ataullakhanov. 2007. In search of an optimal ring to couple microtubule depolymerization to processive chromosome motions. *Proc. Natl. Acad. Sci. USA*, 104:19017-22.

   Web-link: http://www.pnas.org/content/104/48/19017

3. E. L. Grishchuk, I. S. Spiridonov, V. A. Volkov, **A. Efremov**, S. Westermann, D. Drubin, G. Barnes, F. I. Ataullakhanov, and J. R. McIntosh. 2008. Different assemblies of the DAM1 complex follow shortening microtubules by distinct mechanism. *Proc. Natl. Acad. Sci. USA*, 105:6918-23.

   [*F1000 recommendation*]

   Web-link: http://www.pnas.org/content/105/19/6918

4. J.R. McIntosh, E.L. Grishchuk, M. Morphew, **A.K. Efremov**, K. Zhudenkov, V. Volkov, I. Cheeseman, A. Desai, D.N. Mastronarde, F.I. Ataullakhanov. 2008. Fibrils connect microtubule tips with kinetochores: a mechanism to couple tubulin dynamics to chromosome motion. *Cell*, 135:322-33.

   [*F1000 recommendation*]

   Web-link: https://www.cell.com/cell/fulltext/S0092-8674(08)01119-7

5. Ekaterina L. Grishchuk, **Artem K. Efremov**, Vladimir A. Volkov, Ilia S. Spiridonov, Nikita Gudimchuk, Stefan Westermann, David Drubin, Geojana Barnes, J. Richard McIntosh, and Fazly I. Ataullakhanov. 2008. The Dam1 ring binds microtubules strongly enough to be a processive as well as energy-efficient coupler for chromosome motion. *Proc. Natl. Acad. Sci. USA*, 105:15423-8.

   Web-link: http://www.pnas.org/content/105/40/15423

6. **Artem Efremov***, Zhisong Wang*. 2011. Maximum directionality and systematic classification of molecular motors. *Phys. Chem. Chem. Phys.*, 13:5159-5170.

   Web-link: http://pubs.rsc.org/en/content/articlelanding/2011/cp/c0cp02519d/#!divAbstract

7. **Artem Efremov***, Zhisong Wang*. 2011. Universal optimal working cycles of molecular motors. *Phys. Chem. Chem. Phys.*, 13:6223-6233.

   Web-link: http://pubs.rsc.org/en/content/articlelanding/2011/cp/c0cp02118k/#!divAbstract

8. **Artem Efremov***, Jianshu Cao*. 2011. Bistability of cell adhesion in shear flow. *Biophys. J.*, 101:1032-1040.

Web-link: https://www.cell.com/biophysj/fulltext/S0006-3495(11)00884-8

9. Hailong Lu[#], **Artem K. Efremov[#]**, Carol S. Bookwalter, Elena B. Krementsova, Jonathan W. Driver, Kathleen M. Trybus, and Michael R. Diehl. 2012. Collective dynamics of elastically-coupled myosin V motors. *J. Biol. Chem.*, 287:27753-61.

Web-link: http://www.jbc.org/content/287/33/27753

10. Karthik Uppulury, **Artem Efremov**, Jonathan Driver, Kenneth, Jamison, Michael R. Diehl, and Anatoly B. Kolomeisky. 2012. How the interplay between mechanical and non-mechanical interactions affects multiple kinesin dynamics. *J. Phys. Chem. B*, 116:8846-55.

Web-link: https://pubs.acs.org/doi/abs/10.1021/jp304018b

11. Juan Cheng, Sarangapani Sreelatha, Ruizheng Hou, **Artem Efremov**, Ruchuan Liu, Johan R.C. van der Maarel, Zhisong Wang. 2012. Bipedal nanowalker by pure physical mechanisms. *Phys. Rev. Lett.*, 109:238104.

[*Featured in Physics*, *Highlighted by American Physical Society*]

Web-link: https://journals.aps.org/prl/abstract/10.1103/PhysRevLett.109.238104

12. Karthik Uppulury, **Artem K. Efremov**, Jonathan W. Driver, D. Kenneth Jamison, Michael R. Diehl,and Anatoly B. Kolomeisky. 2013. Analysis of cooperative behavior in multiple kinesins motor protein transport by varying structural and chemical properties. *Cell Mol. Bioeng.*, 6:38-47.

Web-link: https://link.springer.com/article/10.1007%2Fs12195-012-0260-9

13. Xiaofeng Xu, **Artem K. Efremov**, Ang Li, Lipeng Lai, Ming Dao, Chwee Teck Lim, Jianshu Cao. 2013. Probing the cytoadherence of malaria infected red blood cells under flow. *PLoS One*, 8:e64763.

Web-link: http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0064763

14. Zhisong Wang, Ruizheng Hou, **Artem Efremov**. 2013. Directional fidelity of nanoscale motors and particles is limited by the 2nd law of thermodynamics – via a universal equality. *J. Chem. Phys.*, 139:035105.

Web-link: https://aip.scitation.org/doi/abs/10.1063/1.4813626?journalCode=jcp

15. **Artem K. Efremov[#]**, Anand Radhakrishan[#], David S. Tsao, Carol S. Brookwalter, Kathleen M. Trybus, and Michael R. Diehl. 2014. Delineating cooperative responses of processive motors in living cells. *Proc. Natl. Acad. Sci. USA*, 111:E334-43.

[*Highlighted by ScienceDaily, Phys.org and several other news outlets*]

Web-link: http://www.pnas.org/content/111/3/E334

16. Xu Yue, Chen Hu, Qu Yu-Jie, **Artem K. Efremov**, Li Ming, Ouyang Zhong-Can, Liu Dong-Sheng, Yan Jie. 2014. Mechano-chemical selections of two competitive unfolding pathways of a single DNA i-motif. *Chin. Phys. B*, 23:068702.

Web-link: http://iopscience.iop.org/article/10.1088/1674-1056/23/6/068702/meta

17. Huijuan You, Xiangjun Zeng, Yue Xu, Ci Ji Lim, **Artem K. Efremov**, Anh Tuan Phan, Jie Yan. 2014. Dynamics and stability of polymorphic human telomeric G-quadruplex under tension. *Nucleic Acids Res.*, 42:8789-95.

Web-link: https://academic.oup.com/nar/article/42/13/8789/1298035

18. Mingxi Yao, Wu Qiu, Ruchuan Liu, **Artem K. Efremov**, Peiwen Cong, Rima Seddiki,

Manon Payre, Lim Chwee Teck, Benoit Ladoux, Rene-Marc Mege, Jie Yan. 2014. Force-dependent conformational switch of alpha-catenin controls vinculin binding. *Nat. Commun.*, 5:4525.

Web-link: https://www.nature.com/articles/ncomms5525

19. Iong Ying Loh, Juan Cheng, Shern Ren Tee, **Artem Efremov**, Zhisong Wang. 2014. From bi-state molecular switches to self-directed track-walking nanomotors. *ACS Nano*, 8:10293-304.

    Web-link: https://pubs.acs.org/doi/abs/10.1021/nn5034983

20. **Artem K. Efremov**, Yuanyuan Qu, Hugo Maruyama, Ci J. Lim, Kunio Takeyasu, Jie Yan. 2015. Transcriptional repressor TrmBL2 from *Thermococcus kodakarensis* forms filamentous nucleoprotein structures and competes with histones for DNA binding in a salt- and DNA supercoiling-dependent manner. *J. Biol. Chem.*, 290:15770-84.

    Web-link: http://www.jbc.org/content/290/25/15770

21. Shimin Le, Mingxi Yao, Jin Chen, **Artem K. Efremov**, Sara Azimi, Mark B. H. Breese, Jie Yan. 2015. Disturbance-free rapid solution exchange for magnetic tweezers single-molecule studies. *Nucleic Acids Res.*, 43:e113.

    Web-link: https://academic.oup.com/nar/article/43/17/e113/2414325

22. **Artem K. Efremov***, Ricksen S. Winardhi, Jie Yan*. 2016. Transfer-matrix calculation of DNA polymer micromechanics under tension and torque constraints. *Phys. Rev. E*, 94:032404.

    [*Editors' suggestion*]

    Web-link: https://journals.aps.org/pre/abstract/10.1103/PhysRevE.94.032404

23. **Artem K. Efremov***, Ricksen S. Winardhi*, Jie Yan*. 2017. Theoretical methods for studying DNA structural transitions under applied mechanical constraints. *Polymers*, 9:74.

    [*Invited review*]

    Web-link: http://www.mdpi.com/2073-4360/9/2/74

24. Miao Yu, Xin Yuan, Chen Lu, Shimin Le, Ryo Kawamura, **Artem K. Efremov**, Zhihai Zhao, Michael Kozlov, Michael Sheetz, Alexander Bershadsky, Jie Yan. 2017. mDia1 senses both force and torque during F-actin filaments polymerization. *Nat. Commun.*, 8:1650.

    Web-link: https://www.nature.com/articles/s41467-017-01745-4

25. **Artem K. Efremov***, Fazoil I. Ataullakhanov*. 2018. Atomic-scale insights into physical mechanisms driving enzymes "working cycles". *Biophys. J.*, 114:2027-9.

    [*Invited commentary letter on "Motor-like properties of non-motor enzymes" paper by Slochower, D. R., and M. K. Gilson., Biophys. J., 2018*]

    Web-link: https://www.cell.com/biophysj/fulltext/S0006-3495(18)30444-2

26. **Artem K. Efremov***, Jie Yan*. 2018. Transfer-matrix calculations of the effects of tension and torque constraints on DNA-protein interaction. *Nucleic Acids Res.*, 46:6504-27.

    Web-link: https://doi.org/10.1093/nar/gky478
    Web-link, pre-print: https://arxiv.org/abs/1802.01437

27. Miao Yu, Shimin Le, **Artem K. Efremov**, Xiangjun Zeng, Alexander Bershadsky, Jie Yan. 2018. Effects of mechanical stimuli on profilin/formin-mediated actin polymerization. *Nano Lett.*, 18:5239-47.

    Web-link: https://pubs.acs.org/doi/10.1021/acs.nanolett.8b02211

28. N. O. Alieva[#], **A. K. Efremov[#]**, S. Hu, D. Oh, M. Natarajan, H. T. Ong, A. Jegou, G. Romet-Lemonne, J. Groves, M. P. Sheetz, J. Yan and A. D. Bershadsky. 2018. Force dependence of filopodia adhesion: involvement of myosin II and formins. *Submitted*. Pre-print, BioRxiv doi: https://doi.org/10.1101/195420.

Web-link: https://www.biorxiv.org/content/early/2017/09/28/195420

29. Shiwen Guo, **Artem K. Efremov** and Jie Yan. 2018. The force-dependent rate of strand-peeling transition. *Submitted*.

* – corresponding author

# – equal contribution.

Total number of citations, Google Scholar: 1121

Web-link to ORCID: ORCID

H-index, Google Scholar: 16

Teaching statement

Cells are the basic structural and biological units of all known living organisms. Maintenance of the cell structure as well as proper cell functioning is based on an intricate synergetic cooperation between a large number of highly nonlinear molecular processes, understanding of which requires a multidisciplinary approach based on combination of *in vivo* molecular biology methods, *in vitro* single-molecule manipulation techniques and advanced theoretical modeling. Such interplay between theory and experiment is the central part of the contemporary philosophy in biophysical studies, which allows one to gain detailed insights into the underlying molecular mechanisms governing behavior of various subcellular systems and organelles. I believe that this approach should be learned by all students who are planning to do research in biophysics and molecular biology fields.

As a result, the main goal of my part of the Advanced Biophysics lecture course (PC5213), which I have been teaching for two years to Master and PhD degree students in Faculty of Science, National University of Singapore, is to acquaint its attendees with the major theoretical and experimental methods being used in the modern single-molecule biophysics field, and to demonstrate how their combination can be applied for detailed investigation of complex cellular systems on a number of real examples. This approach both reveals basic principles behind contemporary single-molecule experimental methods and demonstrates to students the role of physical laws in molecular processes that take place in living cells, illustrating how seemingly abstract physical concepts are literally manifested in life itself.

The lecture course has got many positive feedbacks from the students who attended it, making it one of the most popular teaching modules among of level 5 university courses (highest university level) taught to Master and PhD students at National University of Singapore, Physics Department.

Aims and objectives of the teaching course

During the course of the module, students learn a number of important theoretical concepts from the fields of physical chemistry, chemical kinetics and non-linear dynamics as well as the major experimental single-molecule manipulation methods, which are widely used in modern single-molecule biophysical studies. Based on the examples of mechanosensing protein complexes, intracellular transport system, DNA organization by architectural proteins and genetic toggle switches it is demonstrated how the combination of these methods can be applied to study subcellular biological systems to get deep insights into the underlying molecular processes, revealing the major working principles of cellular systems.

Objectives:

1. To familiarize students with the main theoretical and experimental methods used in single-molecule biophysical studies.
2. To develop understanding of the major physical principles governing physicochemical processes in living cells.
3. To build foundation for future theoretical and/or experimental research in molecular biology and biophysics fields.

Syllabus

1. Basic concepts of the chemical kinetics theory. Rate of a chemical reaction. Law of mass action. Equilibrium constant. Chemical potential. Ideal solution. Connection between the equilibrium constant, reaction quotient and standard Gibbs free energy of the reaction.

Equilibrium dissociation constant. Buffer solutions. Van’t Hoff plot. DNA base-pairing energy.

2. Non-equilibrium processes. Activated complex theory. Arrhenius equation. Kinetic graph and its master equation. Numeric and analytic methods for solving the master equation in non-steady state and steady state cases (Runge-Kutta and Gellispie algorithms, Cramer’s rule, chemical graphs and trees method). Michaelis-Menten kinetics. Cooperativity. Hill equation.
3. Experimental methods in single-molecule biophysics – atomic force microscopy, optical and magnetic tweezers. Single-molecule manipulation and microparticle tracking techniques. Force-spectroscopy methods for studying force-dependent states and structural transitions of biomolecules.
4. Energy transduction in biological systems. Energy efficiency and entropy production. Chemical fluxes and the cycle balance equation. Intracellular transport in living cells. Cell cytoskeleton and motor proteins. Kinesin working cycle and simple kinetic models describing it. Kinesin stepping ratio and force-velocity curves.
5. DNA conformation in the absence and presence of various mechanical constraints. Freely jointed chain and worm-like chain polymer models. Metropolis-Monte Carlo algorithm. DNA organization by architectural proteins. Transfer-matrix calculations.
6. Basic concepts of the nonlinear dynamics theory. System bottlenecks, time hierarchy and slowly changing variables. Tikhonov theorem. System phase portrait. Fixed points and their types. Isolcines. Geometric approaches to understanding dynamics of nonlinear systems. Genetic toggle switches and their role in regulation of cells / viruses development. Application of genetic toggle switches in synthetic biology.