Konstantin I. Popov, Ph.D.

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Experienced scientist with training in multidisciplinary areas in physics, chemistry, mathematics, biophysics, computer and material science. My research focuses on experimental and computational structural biology, cheminformatics and computational drug discovery, fundamental aspects of protein allostery, force fields and software development with the emphasis on research strategy and methodology design along with experimentally testable hypothesis generation.

As an accomplished faculty and academic researcher, I have co-authored research proposals in the areas of biophysics and drug discovery and published 20+ original peer-reviewed articles. I have trained three graduate students and four postdocs. As a research associate in oilfield industry, I have co-invented multiple technologies covered in nine USA, Canadian and Russian patents.

AREAS OF EXPERTISE

- Biophysics/Biochemistry
- Computational biology
- Structural biology
- Molecular modeling
- Protein design
- Protein allostery
- Cell motility
- Drug discovery/design
- Molecular docking
- Fragment-based drug design
- AI and DEL assisted lead generation
- Ligand-based drug design
- Cheminformatics
- QSAR
- Physics
- Chemistry
- Physical chemistry
- Statistical mechanics
- Polymer/material science
- Data science
- Statistics

PROFESSIONAL EXPERIENCE

Assistant Professor, Department of Biochemistry & Biophysics, UNC Chapel Hill — Dec. 2014 - present

Leading computational drug discovery team, securing funding for basic research and drug discovery programs in several therapeutic and research areas. Proposing and developing novel research strategies and methodologies for AI-driven drug discovery. Uncovering etiology of protein misfolding related diseases. Performing research focused on integration of computational and experimental methods to study protein structure and allostery. Developing computational approaches to optimize single-chain variable fragments specificity for (CAR)-T cell-based immunotherapies. Supervising undergraduate, graduate students and postdocs. Teaching Molecular structure and dynamics class, training graduate students and postdocs.

Key Contributions:

- Supervised structure-based drug discovery group in a nation-wide antiviral drug discovery project. Discovered, prioritized, and optimized novel chemical probe candidates for: SARS-Cov2 M^{pro}, nsp13, CHIKV nsp2 (orthosteric and allosteric) that are being tested in biophysical, enzymatic and phenotypic assays
- Contributed to the development and implementation of a novel integrative approach for accelerated chemical probe generation. The approach utilizes a combination of X-ray data from fragment soaking and computational characterization of the active site to build an AI-driven generative model for diverse probe candidate generation
- Proposed a strategy and supervised a pilot study for the development of AI-driven approaches to generating diverse sets of readily available drug-like high-affinity hits utilizing the unique data available from DNA-encoded library screening
- Developed an experimentally driven molecular dynamics approach that allowed our team to predict conformational ensembles and identify potential druggable sites for Tau, alpha-synuclein and prion proteins
- Developed and implemented a graph-theoretical methodology for prediction of allosteric hot spots using a combination of experimental and computational data. Mapped allosteric communications between potentially druggable sites in multiple proteins including ion channels.

Postdoctoral Fellow, Department of Chemistry, UMD College Park — Mar. 2011 - Dec. 2014

Developing physical coarse-grained models, advanced computational approaches and software to study processes driving cell motility at multiple scales: from dynamics of single proteins to entire cellular reorganization. Elucidating fundamental processes underlying cancer progression on cellular level. Studying physical aspects of capsid formation.

Key Contributions:

- Developed a pioneering approach to theoretically and computationally characterize a coupling between mechanical process generated by molecular motors and cytosolic proteins in the cytoskeleton and chemical reactions occurring inside a cell
- Implemented and optimized the software package “MEDYAN”, a state-of-the-art computational tool capable of describing properties of cytoskeleton networks with molecular level of resolution.

Junior Postdoctoral Fellow, Materials Science & Engineering, Northwestern University Dec. 2009 - Mar. 2011

Modeling and developing new classes of nano-materials that can change their properties in response to external/environmental stimuli. Designing functionalized nano-particles and studying their self-assembly for medical applications.

Key Contributions:

- Demonstrated the anisotropic degree of ionization of the coated nano-particles interacting in aqueous salt solution that can be used to design and control aggregates with novel and unexpected symmetries.

Research Associate, Schlumberger Moscow Research, Russia Dec. 2006 - Nov. 2009

Conducting research in a cross-functional team comprised of scientist, engineers and product developers focused on introduction and commercialization of novel products for oilfield services. Developing and patenting (9 patents) new technologies and materials for enhanced oil recovery techniques.

Key Contributions:

- Designed experimental setups, collected data and built models for gel-fiber suspension flow and isolation plugs formation that helped Schlumberger in developing a multibillion HiWay fracturing technology
- Co-invented a technology that allows to decrease an effective viscosity in a fluid flow by applying a modulated multi-frequency or stochastic acoustic impact.

EDUCATION & CREDENTIALS

Ph.D. - Polymer Science, Moscow State University, Moscow, Russia **2009**

Dissertation: *Studying self-assembly of macromolecules with complex architecture on the surface.*

M.S. - Physics, Moscow State University, Moscow, Russia **2006**

AWARDS

Junior Faculty Development Award, UNC **2018**

TECHNICAL SKILLS

- Numerical analysis, scientific computing, molecular modeling, mathematical modeling, stochastic modeling
- Data curation, exploratory data analysis, QSAR modelling, regression models, machine learning
- Proficient programming skills and computational analysis background (e.g. C++, Python, Fortran, Jupyter notebook)
- Proficient in standatd molecular modeling and design tools (e.g. GROMACS, VMD, PyMol, Schrodinger, KNIME, OpenEye)
- Scientific hypotheses generation and design of methodologies for their testing
- Management of multidisciplinary scientific teams and collaborations
- Scientific writing (publications, reports, grants), public speaking, peer reviews.

PUBLICATIONS AND PATENTS

- Popov KI, Potemkin II. “Two mechanisms of spontaneous curvature of strongly adsorbed (2D) double comblike copolymers.” *Langmuir*. 2007 Jul 17;23(15):8252-6. doi: 10.1021/la070035d. Epub 2007 Jun 20. PubMed PMID: 17580916.
- Potemkin II, Popov KI. “Effect of grafting density of the side chains on spontaneous curvature and persistence length of two-dimensional comblike macromolecules.” *J Chem Phys*. 2008 Sep 28;129(12):124901. doi: 10.1063/1.2980050. PubMed PMID: 19045059.
- D.A. Koroteev, K.I. Popov and O.N. Zhuravlev, “Decrease of hydrodynamic resistance at stochastic treatment of the flow*.”, Applied Physics (Russian)*, 2008 No. 2.
- Popov KI, Palyulin VV, Möller M, Khokhlov AR, Potemkin II. “Surface induced self-organization of comb-like macromolecules.” *Beilstein J Nanotechnol.* 2011;2:569-84. doi: 10.3762/bjnano.2.61. Epub 2011 Sep 12. PubMed PMID: 22003463; PubMed Central PMCID: PMC3190627.

- Popov KI, Nap RJ, Szleifer I, Olvera de la Cruz M." Interacting nanoparticles with functional surface groups. Journal of polymer science." *Part B, Polymer physics.* 2012 April; 50:852-862. doi: DOI: 10.1002/polb.23077.
- Popov KI, Papoian GA. "Capsid deformations reveal complex mechano-chemistry." *Biophys J.* 2013 Nov 19;105(10):2233-4. doi: 10.1016/j.bpj.2013.09.055. PubMed PMID: 24268133; PubMed Central PMCID: PMC3838748.
- Popov K, Komianos J, Papoian GA. "MEDYAN: Mechanochemical Simulations of Contraction and Polarity Alignment in Actomyosin Networks". *PLoS Comput Biol.* 2016 Apr;12(4):e1004877. doi: 10.1371/journal.pcbi.1004877. eCollection 2016 Apr. PubMed PMID: 27120189; PubMed Central PMCID: PMC4847874.
- Politi R, Convertino M, Popov K, Dokholyan NV, Tropsha A. "Docking and Scoring with Target-Specific Pose Classifier Succeeds in Native-Like Pose Identification But Not Binding Affinity Prediction in the CSAR 2014 Benchmark Exercise." *J Chem Inf Model.* 2016 Jun 27;56(6):1032-41. doi: 10.1021/acs.jcim.5b00751. Epub 2016 Apr 20. PubMed PMID: 27050767.
- Brodie NI, Popov KI, Petrotchenko EV, Dokholyan NV, "Borchers CH. Solving protein structures using short-distance cross-linking constraints as a guide for discrete molecular dynamics simulations." *Sci Adv.* 2017 Jul;3(7):e1700479. doi: 10.1126/sciadv.1700479. eCollection 2017 Jul. PubMed PMID: 28695211; PubMed Central PMCID: PMC5501500.
- Shobair M, Popov KI, Dang YL, He H, Stutts MJ, Dokholyan NV. "Mapping allosteric linkage to channel gating by extracellular domains in the human epithelial sodium channel." *J Biol Chem.* 2018 Mar 9;293(10):3675-3684. doi: 10.1074/jbc.RA117.000604. Epub 2018 Jan 22. PubMed PMID: 29358325; PubMed Central PMCID: PMC5846138.
- Zhang Y, Hashemi M, Lv Z, Williams B, Popov KI, Dokholyan NV, Lyubchenko YL. "High-speed atomic force microscopy reveals structural dynamics of α-synuclein monomers and dimers." *J Chem Phys.* 2018 Mar 28;148(12):123322. doi: 10.1063/1.5008874. PubMed PMID: 29604892; PubMed Central PMCID: PMC5764752.
- Brodie NI, Popov KI, Petrotchenko EV, Dokholyan NV, Borchers CH. "Conformational ensemble of native α-synuclein in solution as determined by short-distance crosslinking constraint-guided discrete molecular dynamics simulations." *PLoS Comput Biol.* 2019 Mar;15(3):e1006859. doi: 10.1371/journal.pcbi.1006859. eCollection 2019 Mar. PubMed PMID: 30917118; PubMed Central PMCID: PMC6453469.
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- Reilley DJ, Popov KI, Dokholyan NV, Alexandrova AN. "Uncovered Dynamic Coupling Resolves the Ambiguous Mechanism of Phenylalanine Hydroxylase Oxygen Binding." *J Phys Chem B.* 2019 May 30;123(21):4534-4539. doi: 10.1021/acs.jpcb.9b02893. Epub 2019 May 17. PubMed PMID: 31038957.
- Sapienza PJ, Popov KI, Mowrey DD, Falk BT, Dokholyan NV, Lee AL. "Inter-Active Site Communication Mediated by the Dimer Interface β-Sheet in the Half-the-Sites Enzyme, Thymidylate Synthase.", *Biochemistry.* 2019 Jul 30;58(30):3302-3313. doi: 10.1021/acs.biochem.9b00486. Epub 2019 Jul 18. PubMed PMID: 31283187; PubMed Central PMCID: PMC7110413.
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- Yoshino H, Yin G, Kawaguchi R, Popov KI, Temple B, Sasaki M, Kofuji S, Wolfe K, Kofuji K, Okumura K, Randhawa J, Malhotra A, Majd N, Ikeda Y, Shimada H, Kahoud ER, Haviv S, Iwase S, Asara JM, Campbell SL, Sasaki AT. "Correction: Identification of lysine methylation in the core GTPase domain by GoMADScan." *PLoS One.* 2019;14(10):e0224443. doi: 10.1371/journal.pone.0224443. eCollection 2019. PubMed PMID: 31639175; PubMed Central PMCID: PMC6805050.
- Popov KI, Makepeace KAT, Petrotchenko EV, Dokholyan NV, Borchers CH. "Insight into the Structure of the "Unstructured" Tau Protein." *Structure.* 2019 Nov 5;27(11):1710-1715.e4. doi: 10.1016/j.str.2019.09.003. Epub 2019 Oct 15. PubMed PMID: 31628033.

- Makepeace KAT, Brodie NI, Popov KI, Gudavicius G, Nelson CJ, Petrotchenko EV, Dokholyan NV, Borchers CH. "Ligand-induced disorder-to-order transitions characterized by structural proteomics and molecular dynamics simulations." *J Proteomics.* 2020 Jan 16;211:103544. doi: 10.1016/j.jprot.2019.103544. Epub 2019 Nov 1. PubMed PMID: 31683063; PubMed Central PMCID: PMC6878985.
- Bobrowski T, Melo-Filho CC, Korn D, Alves VM, Popov KI, Auerbach S, Schmitt C, Moorman NJ, Muratov EN, Tropsha A. "Learning from history: do not flatten the curve of antiviral research!" *Drug Discov Today.* 2020 Sep;25(9):1604-1613. doi: 10.1016/j.drudis.2020.07.008. Epub 2020 Jul 15. Review. PubMed PMID: 32679173; PubMed Central PMCID: PMC7361119.
- Jason J. Serpa, Konstantin I. Popov, Evgeniy V. Petrotchenko, Nikolay V. Dokholyan, and Christoph H. Borchers, "Structure of prion β-oligomers as determined by short-distance crosslinking constraint-guided discrete molecular dynamics simulations", Proteomics, Sept 2021, PMID: 34482645 , DOI: 10.1002/pmic.202000298
- V. R Chirasani, K. I Popov, G. Meissner, N. V Dokholyan, "Mapping Co-regulation Pathways among Ligand Binding sites in RyR1", Proteins, PMID: 34455637 PMCID: PMC8738105 DOI: 10.1002/prot.26228
- Cleber Melo-Filho, Tesia Bobrowski, Holli-Joi Martin, Zoe Sessions, Konstantin I. Popov, Nathaniel J. Moorman, Ralph S. Baric, Eugene Muratov, Alexander Tropsha, "Conservation of coronavirus proteins is a key to broad-spectrum antivirals.", Antiviral Research, Aug 2022, PMID: 35691424 DOI: 10.1016/j.antiviral.2022.105360

Patents:

- US 7789141 "Oil recovery enhancement method", O. Zhuravlev, D. Koroteev, K. Popov
- CA 2616575 "Oil recovery enhancement method", O. Zhuravlev, D. Koroteev, K. Popov
- US 2011/0100625A1 "Method for forming an isolating plug", K.I. Popov, V.K. Khlestkin
- RU 2380530 "Method for prevening gas-hydrate formation", O. Zhuravlev, D. Koroteev, K. Popov, D.Bagrets
- RU 2355878 "Method for increasing reservoir recovery", O. Zhuravlev, D. Koroteev, K. Popov
- RU 2350830 "Method of transporting viscous oil and oil products via pipeline (versions)", O. Zhuravlev, D. Koroteev, K. Popov
- RU 2393331 "Method of isolating plug formation", K.I. Popov, V.K. Khlestkin
- RU 2412339 "Procedure for treatment of bottomhole reservoir zone (versions)", D. Koroteev, K. Popov
- RU 2411354 "Procedure for treatment of bottomhole reservoir zone", D. Koroteev, K. Popov, S. Irishkov.