# **Evgeni Nikolaev**

### **Computational Biologist and Data Scientist**

Citizenship: The United States



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Currently seeking Computational Systems Biology / Systems Bioinformatics / Genomics Data Science opportunities in biotech companies to develop large-scale data analytic and scalable modeling approaches with implications in biomedical research.

## **Summary of Work Experience**

- Significant experience in problem-solving, rapid and innovative development of expertise in various domains of biology, elector-chemistry, and medicine, including metabolism, immunology of infectious and cancer diseases. Published 50+ technical articles.
- Computational Biology and Bioinformatics applied to Metabolism, Immunology, and Cancer Research with a background in Multi-Physics and Applied Math.
- Data Science using Python, R, SQL and C++ for the entire data analysis workflow and mathematical modeling, including data wrangling, visualization, exploratory data analysis, and applying machine learning models to big data.
- Optimization with lindo@API / glpk API: LP, MILP, MINP, and stochastic simulations (MCMC).

#### **Skills**

**BIOINFORMATICS:** NGS RNA-seq and NAT-seq, WES/WGS, CHIP-seq, gnomAD/ExAc

**MACHINE LEARNING:** Markov chain Monte Carlo (MCMC) methods including: Dynamic Bayesian Networks (DBN), Bayesian Statistics using STAN-3 and PyMC3, Bayesian Hierarchical Mixed-Effect Regression Analysis, Bayesian Mixture Distribution Fitting, Data Cleaning and Missing Value Imputation, Imbalance Classification, kNN, Random Forests, Ensemble Learning, Deep-Learning Time Series Analysis, XGBOOST, Automated Report Generation, etc.

**DATA VISUALIZATION:** Matplotlib, Seaborn, plotly, plotnine, and ggplot2

**REPORT AUTOMATION:** papermil

**CODING:** Bash/Akw/Sed/GNU Parallel, Python/Pandas, R, SQLite, C/C++/STL, MATLAB, and LaTex **APPLIED MATH:** Computational Bifurcation Analysis with Matcont and AUTO, Computational Fluid

Dynamics with Open FOAM

**COMP. GENOMICS CLOUDS:** DNAnexus

CODING ECOSYSTEM: Linux (Ubuntu), DataSpell (PyCharm), and RStudio

## **Experience**

NIH (remote) Oct. 2021 - Current

Position: Genomics Data Scientist (Consultant)

*Project:* NGS RNA-seq and NAT-seq Pipeline Development with DNA Nexus

**Air-Force Research Laboratory** (Dayton, OH) May 2019 – Oct. 2021

Position: Lead Scientist (UES contr.)

Project: "Connecting Multi-Omics Dots on the Human Gut-Brain Axis."

*Challenge:* Development of probabilistic data-fusion approaches to integrate and interpret heterogeneous data obtained by several research teams.

*Approaches:* Various bioinformatics and machine learning approaches, including probabilistic methods, times series, dimensionality reduction, etc.

Deliverables:

- (1) Bayesian (MCMC) mixture distribution and mixed effect based analyses of and fitting noise sources in flow cytometry experiments (time series);
- (2) Development of CFD models of multiphysics phenomena in microfluidic chips using OpenFOAM;
- (3) Installation and development of NGS RNAseq computational genomics pipelines on stand-alone Linux/Ubuntu.21.10 workstations;
- (4) Serval manuscripts are in preparation for submission.

#### Rutgers Cancer Institute of New Jersey (New Brunswick, NJ)

*May 2017 – Current* 

Position: Member II

*Project:* "Immunobiochemical Reconstruction of Influenza Lung Infection Melanoma Skin Cancer interactions:" Understanding of a previously unrecognized acute non-oncogenic infection factor contributing to increased infection-related death incidences in patients with cancer.

*Challenge:* Inference of signals from sparse heterogeneous data obtained from mice with different types of tumors and infections, including wounds, to reconstruct signaling pathways and gene-regulatory networks compatible with death incidence observations.

*Approaches:* Development of a series of falsifiable ODE mechanistic mathematical models used to recognize and interpret relevant signals mechanistically.

*Deliverables:* A previously unrecognized acute non-oncogenic infection factor is recognized and published in a high-profile immunological journal; the results also point to dangerous side effects of oncolytic viruses (OVs) treatments.

**Center for Quantitative Biology, Rutgers University** (Piscataway, NJ) *Jan. 11 - Dec. 18 Position:* Quantitative Biologist

*Project 1: "Understanding of tuberculosis (TB) induced changes in metabolism leading to the accumulation of cholesterol in the lungs of infected patients"* 

*Challenge:* Inference of signals from highly noisy sparse heterogeneous lipid data obtained from patients' sputum, TB-infected lungs of macaques, and *in-vitro* studies of cell cultures with irradiated *M. tuberculosis* (*Mtb*) bacteria

Approaches: Cluster analyses Deliverables: A publication

Project 2: "Mathematical modeling of cell-free TX-TL circuits"

*Challenge:* Development of the smallest mathematical model to capture both weak and strong signals seen in 32 sets of dense experimental measurements

*Approaches:* Application of Machine Learning (ML) techniques (MCMC) implemented in Python, and R to automate the model construction and analysis

*Technology*: a Stan-based MCMC approach is used to fit the model to 32 dense datasets using hyper-parameter and mixed-effect approaches, while ML regression is used to detect changes and trends in the parameter values depending on the experimental conditions (e.g., DNA concentration and proteases) *Deliverables*: a modeling framework and publications

Project 3: "Biosensors based on bacterial (E. coli) genetic toggles"

*Technology*: Bifurcation analysis tools, matcont (Matlab) and Auto-7 (parallel Fortran)

*Deliverables*: (1) developed mathematical approaches to study synchronization of synthetic genetic toggles via common medium; and (2) publications

**Dept. of Cell Biology, Thomas Jefferson University** (Philadelphia, PA) May 07 - Dec. 10

Position: Research Associate

*Project:* "Modeling molecular mechanisms of hypertension"

Technology: Python and Python-based SMBL API

Deliverables: (1) developed a model of GPCR signaling pathway in Rat's Nucleus Tractus Solitarius

(NTS) - Gateway to Neural Circulatory Control, and (2) publications

**Dept. of Biomedical Engineering, Cornell Univ.** (Ithaca, NY)

Feb. 05 - Apr. 07

Position: Research Associate

Project: "Development of the Cornell Computer Model of a Minimal Living Cell"

Technology: Matlab

Deliverables: (1) extended the Cornell E. Coli Computer Model, and (2) publications

**Dept. of Chemical Engineering, The Penn. State Univ.** (State College, PA)

Sept. 02 – Jan. 05

Position: Research Scholar

*Project:* "Development of scalable computer tools for the analysis of metabolic reconstructions of annotated bacterial genomes"

Technology: libLindo API & C++/STL, and Matlab

*Deliverables*: (1) developed computational tools to study genome-scale stoichiometric matrices; (2) developed computational tools to optimize production of useful proteins using large-scale kinetic

models of bacterial cells; and (3) wrote papers

**Integrated Genomics, Inc.** (Chicago, IL)

Jul. 1999 – Aug. 2002

Position: Team Lead and Metabolic Designer

*Project*: "Automation of research and development in bacterial biotechnology"

Technology: libLindo API & C++/STL

Deliverables: Responsible for hiring and leading a team of code developers to deliver a modeling

platform

### **Education**

PhD N.V Lobachevsky Nizhny Novgorod State University, Nizhny Novgorod, Russia

1995 Advised by Professor Emmanuil E. Shnol, Institute for Mathematical Problems in Biology, Russian Academy of Sciences, Pushchino Research Center, Pushchino, Moscow Reg., Russia Thesis: "Bifurcation of limit cycles in ODE with finite symmetry group."

MS Moscow Engineering-Physics Institute, Moscow, Russia (Red Diploma with Distinction)

1986 Advised by Professor Emmanuil E. Shnol, Research Computing Center, USSR Academy of Sciences, Pushchino Center for Biological Research, Pushchino, Moscow Reg., Russia Thesis: "*Mathematical modeling of non-growing cell populations.*"

# **Selected publications**

**Nikolaev, E.V.**, Zloza, A., and Sontag, E.D. [2019], "Immunobiochemical Reconstruction of Influenza Lung Infection - Melanoma Skin Cancer Interactions," *Front Immunol* 10 (4): 1-15

**Nikolaev, E.V.,** Rahi, S.J., and Sontag, E.D. [2018], "Subharmonics and chaos in simple periodically-forced biomolecular models," *Biophys J* 114(5): 1232-1240

**Nikolaev, E.V.,** and Sontag, E.D. [2016], "Quorum-Sensing Synchronization of Synthetic Toggle Switches: A Design Based on Monotone Dynamical Systems Theory," *PLoS Comput Biol* 12(4): e1004881

- Skataric, M., **Nikolaev**, **E.V.**, and Sontag, E.D. [2015], "A fundamental limitation of the instantaneous approximation in fold-change detection models," *IET Syst Biol*, Vol. 9(1): 1-15
- Shnol, E.E., **Nikolaev, E.V.,** Selkov, E.E., and Nazarenko, V.G. [2013] "Mathematical modeling of self-synchronization of cell clocks in a non-growing cell population," *VINITI*, UDK 577.31/517.25 N7180-B86, 1-52,
- **Nikolaev, E.V.,** Pine, R., Gennaro, M.L., and Sontag, E.D. [2011], "Mathematical modeling describes a novel bistable mechanism of lipid body formation in macrophages infected with M. tuberculosis," The Fifth Annual 2011 q-bio Conference on Cellular Information Processing, Los Alamos National Laboratory, St. John's College, Santa Fe, NM
- **Nikolaev, E.V.** [2010], "The elucidation of metabolic pathways and their improvements using stable optimization of large-scale kinetic models of cellular systems," *Metab Eng* 12, 26-38
- Atlas, J.C., **Nikolaev, E.V.**, Browning, S.T., and Shuler M.L. [2008], "Incorporating Genome-Wide DNA Sequence Information into a Dynamic Whole-Cell Model of Escherichia coli: Application to DNA Replication," *IET Syst Biol* 2(5), 369 382
- **Nikolaev, E.V.**, Atlas, J.C., and Shuler M.L. [2007], "Sensitivity and control analysis of periodically forced reaction networks using the Green's function method," *J. Theor Biol*, 247(3), 442-461
- **Nikolaev, E.V.**, Atlas, J.C., and Shuler M.L. [2006], "Computer models of bacterial cells: from generalized coarse-grained to genome-specific modular models," *J Phys Conf Ser* 46, 322-326
- **Nikolaev, E.V.**, Burgard, A.P., and Maranas, C.D. [2005], "Elucidation and structural analysis of conserved pools for genome-scale metabolic reconstructions," *Biophys J* 88(1), 37-49
- Burgard, A.P., **Nikolaev, E.V.**, Schilling, C.H., and Maranas, C.D. [2004], "Flux coupling analysis of genome-scale metabolic network reconstructions," *Genome Res* 14, 301-312
- Pharkya, P., **Nikolaev, E.V.**, and Maranas, C.D. [2003], "Review of the Brenda enzymes database," *Metab Eng* 5, 71-73
- Shnol', E.E., and **Nikolaev, E.V.** [1999], "On the bifurcations of equilibria corresponding to double eigenvalues," *Sbornik: Mathematics* 190 (9-10), 1353-1376
- **Nikolaev, E.V.,** and Shnol, E.E. [1998], "Bifurcations of cycles in systems of differential equations with a finite symmetry group I & II," *Journal of Dynamical and Control Systems* 4(3), 315-342, 343-364
- **Nikolaev, E.V.,** Biktashev, V.N., and Holden, A.V. [1998], "On feedback resonant drift and interaction with the boundaries in circular and annular excitable media," *Chaos, Solitons and Fractals* 9(3), 363-376
- **Nikolaev E.V.** [1995] "Bifurcations of limit cycles of differential equations admitting an involutive symmetry," *Sbornik: Mathematics* 186(3-4), 611-627
- Cymbalyuk, G.S., **Nikolaev, E.V.,** and Borisyuk, R.M. [1994], "In-phase and anti-phase self- oscillations in a model of two electrically coupled pacemakers," *Journal of Biological Cybernetics* 71, 153-160
- Khibnik, A.I., Kuznetsov, Yu.A., Levitin, V.V., and **Nikolaev, E.V.** [1993], "Continuation techniques and interactive software for bifurcation analysis of ODEs and iterated maps," *Physica D* 62, 360-371
- Denisov, G.A., Kalyuta, V.K., **Nikolaev, E.V.,** Tischenko, G.A., and Shataeva, L.K. [1993], "Modeling of coupled transport of ions and zwitterions across porous ion exchange membranes," *Journal of Membrane Science* 79, 211-226
- Denisov, G.A., Kalyuta, V.K., and **Nikolaev, E.V.** [1990], "Formation of an electric-potential jump in a weakly dissociating ion-exchange membrane located between acidic and basic electrolytes," *Proceedings of the USSR Academy of Sciences*, Plenum Publishing Corporation, 315(1), 132-136