## BIOGRAPHICAL SKETCH

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NAME: Blinov, Michael L.

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

POSITION TITLE: Assistant Professor of Genetics and Developmental Biology

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.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Moscow State University, Moscow, Russia | B.Sc. | 06/1995 | Mathematics |
| Weizmann Institute of Sciences, Rehovot, Israel | M.Sc. | 06/1997 | Mathematics |
| Weizmann Institute of Sciences, Rehovot, Israel | Ph.D. | 04/2003 | Mathematics |
| Los Alamos National Laboratory, NM, USA | Research Assistant | 04/2003 | Theoretical Immunology |
| Los Alamos National Laboratory, NM, USA | Postdoctoral | 07/2006 | Theoretical Immunology |

### A. Personal Statement

I'm working on integration of different tools into the VCell modeling software. I'm a Ph.D. in Math that worked on algorithms and software development (two patent applications for rule-based modeling algorithms submitted by the Los Alamos National Laboratory) and got extensive experience in cell biology. Being trained as a mathematician, I became fascinated by biology and switched my career by coming to Los Alamos to work on algorithms for computational biology. I am one of the inventors of rule-based modeling approach and developer of BioNetGen software that is now one of the most popular rule-based modeling tools. Realizing that algorithm development needs to be guided by application to real biological systems, I started doing modeling of biological systems. I joined the University of Connecticut Medical School to bridge theoretical science and the needs of translational medicine. I initiated bringing several new modeling methods to VCel, such as rule-based modeling and database resources-driven modeling. My completed algorithmic and software projects within VCell include: enabling rule-based modeling in VCell (VCell 6.1 released 05/2017), providing access and modeling using Pathway Commons collection of databases (VCell 4.8 released 03/2011), using SABIO-RK database of reaction kinetics (VCell 5.2 released 09/2013). Education is a significant part of my efforts. I'm an associate director of a Cell Analysis Modeling area of concentration within Biomedical Sciences Graduate Program, I initiated and teach "Introduction to Systems Biology". The modeling and simulation methods I developed are used for teaching of graduate courses. Many of my projects are collaborative projects among large groups of researchers with different expertise. To this end, I'm spending a significant amount of efforts on smooth integration of diverse tools and data sources, which is complicated by different formats used: VCell and BioNetGen have proprietary XML standards, while Pathway Commons is based on BioPAX standard. I'm working on tools and techniques to provide seamless exchange of data and models encoded in BioPAX, SBML, VCML and BNGL. These are highly collaborative efforts. I was one of the organizers of the 2007 Workshop on Rule Based Modeling, 2007 Workshop on SBML Model Composition and Aggregation and 2010 ICSB Workshop on Advanced Modeling and Simulation Techniques, and 2013 Workshop on Resources for Modeling in Biology.

1. C.V. Falkenberg., J.H. Carson, & **M.L. Blinov**. (2017). Multivalent Molecules as Modulators of RNA Granule Size and Composition. Biophys. J. 113(2): 235-245. PMID: 28242011

2. **M.L. Blinov**, J.C. Schaff, D. Vasilescu, I.I. Moraru, J.E. Bloom & L.M. Loew. (2017) Compartmental and spatial rule-based modeling with Virtual Cell (VCell). Biophys. J. 113, October 3.
3. J.C. Schaff, D. Vasilescu, I.I. Moraru & L.M. Loew, & **M.L. Blinov** (2016) Rule-based modeling with Virtual Cell. *Bioinformatics* 32(18), 2880-2. PMID: 27497444
4. **M.L. Blinov**, J.C. Schaff, O. Ruebenacker, X. Wei, D. Vasilescu, F. Gao, F. Morgan, I.I. Moraru & L.M. Loew. (2014). Pathway Commons at Virtual Cell: use of pathway data for mathematical modeling. *Bioinformatics* 30(2), 292-4. PMID: 24273241
5. **M. L. Blinov**, J. R. Faeder, B. Goldstein and W. S. Hlavacek (2004) BioNetGen: software for rule-based modeling of signal transduction based on the interactions of molecular domains. *Bioinformatics* 20, 3289-3291. PMID: 15217809

## B. Positions and Honors

### Positions and Employment

| | |
|---|---|
| 1999-2001 | Teaching Assistant, Weizmann Institute of Sciences, Rehovot, Israel |
| 2001-2003 | Graduate Research Assistant, Theoretical Biology and Biophysics Group, Theoretical Division, Los Alamos National Laboratory, Los Alamos, NM |
| 2003-2006 | Postdoctoral Research Associate, Theoretical Biology and Biophysics Group, Theoretical Division, Los Alamos National Laboratory, Los Alamos, NM |
| 2006-present | Assistant Professor, Department of Genetics and Developmental Biology, University of Connecticut School of Medicine, Farmington, CT |

### Honors

| | |
|---|---|
| 1994-1995 | International Science Foundation Student Grant for distinguished successes in studies |
| 1994-1995 | International Science Foundation Research Grant #MQO000, PI V. Vasiliev |
| 1995-2002 | Weizmann Institute of Sciences Fellowships |
| 1999 | The National Academy of Sciences (US) Travel Grant |
| 2003 | Student Distinguished Performance Award, Los Alamos National Laboratory |
| 2004 | R&D 100 nomination for BioNetGen software, Los Alamos National Laboratory |
| 2007 | First Runner-Up for the Inter/Multidisciplinary Research Paper Award, IEEE BIBE |
| 2007-2017 | Certificates of Recognition for the teaching program in Community Based Education |

## C. Contribution to Science

### 1. Algorithms and software for rule-based modeling

**Significance:** Signal transduction networks often exhibit combinatorial complexity: the number of protein complexes and modification states that potentially can be generated during the response to a signal is large, because signaling proteins contain multiple sites of modification and interact with multiple binding partners. The conventional approach of manually specifying these networks is error-prone. If the number of species is large enough, manual specification becomes impossible. Reduction in the number of species and reactions is usually based on hidden assumptions that are often unjustified. An alternative to the conventional approach is a rule-based description, where all potential chemical species and reactions in the model are generated automatically by a computer algorithm from a set of rules.

**Role:** I am one of the developers of the rule-based modeling method and software BioNetGen. BioNetGen specification language can describe a broad range of biological effects. Currently, I'm working in close collaboration with Virtual Cell team. I'm developing rule-based applications for modeling in VCell mixing reactions and rules. The latest rule-based enabled version of VCell 6.0 software was released in February 2016, this was a culmination of the three years of development for all different aspects – user-interface, back-end algorithms and client- and server- based simulations.

**Related publications**:

a. **M.L. Blinov**, J.C. Schaff, D. Vasilescu, I.I. Moraru, J.E. Bloom & L.M. Loew. (2017) Compartmental and spatial rule-based modeling with Virtual Cell (VCell). Biophys. J. 113, October 3.
b. J.C. Schaff, D. Vasilescu, I.I. Moraru & L.M. Loew, & **M.L. Blinov** (2016) Rule-based modeling with Virtual Cell. Bioinformatics 32(18), 2880-2. PMID: 27497444

c. J. R. Faeder, **M. L. Blinov**, and W. S. Hlavacek (2008) Rule-based modeling of biochemical systems with BioNetGen. In I. V. Maly, editor, Systems Biology, Methods in Molecular Biology. Humana Press, Totowa, NJ. PMID: 19399430
d. W. S. Hlavacek, J. R. Faeder, **M. L. Blinov**, R. G. Posner, M. Hucka, W. Fontana (2006). Rules for modeling signal-transduction systems. Science STKE, re 6. PMID: 16849649

**2. New modeling methods**

**Significance:** Multivalency may lead to the formation of large molecular clusters or polymers even when the individual binding affinities are weak, such as P-granules, mRNA granules, the assembly focal adhesions and the aggregation of receptor signaling platforms. Such interactions lead to the formation of molecular clusters that increase local concentration of biomolecules, potentially triggering signaling events. Because these complexes often have variable composition, we call them pleomorphic ensembles (PEs), to distinguish them from machines, assemblies of strongly and specifically interacting molecules. Large number of molecules in molecular clusters with rapidly changing composition requires new modeling techniques to simulate the dynamics of cluster composition changes.
**Role:** I'm developing new rule-based methods applied to study of pleiomorphic ensembles.

**Related publications:**

a. C.V. Falkenberg, **M.L. Blinov**, and L.M. Loew (2013). Pleomorphic Ensembles: Formation of Large Clusters Composed of Weakly Interacting Multivalent Molecules, Biophys J, 105. PMID: 24314076
b. B.J Mayer, **M.L. Blinov** and L.M. Loew (2009). Molecular Machines or Pleiomorphic Ensembles: Signaling Complexes Revisited. J Biol, 8(9):81. PMID: 19835637
c. W. Hlavacek, J. Faeder, M. Blinov (2007). Graphical rule based modeling of biochemical networks. US Patent Application US 20070212719 A1
d. **M. Blinov**, J. Faeder, W. Hlavacek (2004). Rule-based modeling of biochemical networks. US Patent Application US 20050042663 A1

**3. Mechanistic computational modeling of signal transduction**

**Significance:** Detailed mechanistic modeling of signal transduction network in a single cell describes activities and interactions among domains of biomolecules (e.g. phosphorylation of specific tyrosine residues, interactions between SH2 domain and phosphotyrosine).
**Role:** I helped in development of several signaling models including Epidermal Growth Factor Receptor signaling, immunoreceptors and cell cycle.

**Related publications:**

a. C.V. Falkenberg, J.H. Carson, & **M.L. Blinov** (2017). Multivalent Molecules as Modulators of RNA Granule Size and Composition. Biophysical Journal. 113(2):235-245. PMID: 28242011
b. Nag, A., Monine, M. I., **Blinov, M. L**., & Goldstein, B. (2010). A Detailed Mathematical Model Predicts That Serial Engagement of IgE–FcεRI Complexes Can Enhance Syk Activation in Mast Cells. J. Immunol, 185, 3268-3276. PMID: 20733205
c. **M.L. Blinov**, J.R. Faeder, B. Goldstein & W.S. Hlavacek (2006). A network model of early events in epidermal growth factor receptor signaling that accounts for combinatorial complexity. BioSystems 83, 136-151. PMID: 16233948
d. J. R. Faeder, W. S. Hlavacek, I. Reischl, **M. L. Blinov**, H. Metzger, A. Redondo, C. Wofsy and B. Goldstein (2003) Investigation of early events in FceRI-mediated signaling using a detailed mathematical model. J. Immunol. 170, 3769-3781. PMID: 12646643

**4. Using data in modeling**

**Significance:** Biological research is becoming increasingly complex and data-rich, with multiple public databases providing a variety of resources: hundreds of thousands of substances and interactions, hundreds of ready to use models, controlled terms for locations and reaction types, links to reference materials (data and/or publications), etc. Mathematical modeling should take advantage of this complex data and create quantitative, testable predictions based on the current state of knowledge.
**Role**: I'm working within Virtual Cell (VCell) modeling and simulation framework in order to help connect the modeling community with the web of machine-processable systems biology knowledge.

**Related publications**:

a. **M.L. Blinov**, J.C. Schaff, O. Ruebenacker, X. Wei, D. Vasilescu, F. Gao, F. Morgan, I.I. Moraru & L.M. Loew. (2014). Pathway Commons at Virtual Cell: use of pathway data for mathematical modeling. Bioinformatics, btt660. PMID: 24273241
b. O. Ruebenacker, I.I.Moraru, J.C.Schaff, **M.L.Blinov** (2009 ) "Integrating BioPAX knowledge with SBML models", IET Systems Biology, 3(5), 317-328. PMID: 21028923
c. O. Ruebenacker O, **M. Blinov** (2010) "Using views of Systems Biology Cloud: application for model building.", *Theory Biosci.* 130: 45-54. PMID: 20730508
d. Demir E, Cary MP, Paley S, Fukuda K, Lemer C, Vastrik I, Wu G, D'Eustachio P, Schaefer C, Luciano J, Schacherer F, Martinez-Flores I, Hu Z, Jimenez-Jacinto V, Joshi-Tope G, Kandasamy K, Lopez-Fuentes AC, Mi H, Pichler E, Rodchenkov I, Splendiani A, Tkachev S, Zucker J, Gopinath G, Rajasimha H, Ramakrishnan R, Shah I, Syed M, Anwar N, Babur O, **Blinov M**, …, Karp PD, Sander C, Bader GD (2010) BioPAX - A Community Standard for Pathway Data Sharing, Nature Biotechnology 28(9):935-42. PMID: 20829833

**5. Models storage and visualization**

**Significance:** A large mechanistic model (accounting for many species and activities and interactions among domains of biomolecules) is very difficult to store, visualize, or modify. The standard way of representing and visualization as a set of individual species and interactions does not work for large models with hundreds to potentially infinite number of species. Rules provide a very convenient way of molecular interaction data representation.
**Role:** I'm working on development of multiple model storage and visualization methods.

**Related publications**:

a. L.A. Chylek, B. Hu, **M.L. Blinov**, T. Emonet, J.R. Faeder, B. Goldstein, R.N. Gutenkunst, J.M. Haugh, T. Lipniacki, R.G. Posner, J. Yang, W.S. Hlavacek. (2011) "Guidelines for visualizing and annotating rule-based models". Mol Biosyst. 7(10):2779-95 PMID: 21647530
b. Y. Igarashi, E.Heureux, K.S.Doctor, P.Talwar, S.Gramatikova, K.Gramatikoff, Y.Zhang, **M.Blinov**, S.S.Ibragimova, S.Boyd, B.Ratnikov, P.Cieplak, A.Godzik, J.W.Smith, A.L.Osterman, and A.M.Eroshkin (2008). PMAP: databases for analyzing proteolytic events and pathways. Nucleic Acids Res D611-8. doi: 10.1093/nar/gkn683. PMID: 18842634
c. **M. L. Blinov** and I. I. Moraru (2007) XML Encoding of Features Describing Rule-Based Modeling of Reaction Networks with Multi-Component Molecular Complexes. Proceedings of the 7th IEEE International Conference on Bioinformatics and Bioengineering: 987-994. PMID: 21464833
d. **M. L. Blinov**, J. Yang, J. R. Faeder and W. S. Hlavacek (2006) Depicting signaling cascades. Nat. Biotechnol. 24, 137-138. PMID: 16465147

**Complete List of Published Work in MyBibliography:**
http://www.ncbi.nlm.nih.gov/sites/myncbi/1P7n5VChhwyQ6/collections/48182653/public/

**D. Research Support**

**Ongoing Research Support**

P41-GM103313 Loew (PI) 08/01/98 – 04/30/17
National Resource for Cell Analysis and Modeling
Develop and disseminate a computational system for cell biological modeling.
Role: co-I

**Completed Research Support**

R01 GM95485-1 Blinov/Moraru (dual PI) 05/01/11 – 04/30/14
Bringing BioNet Rule-Based Modeling to Virtual Cell users
The major goal of this project is to develop an integrated framework for building, simulating, and visualizing rule-based models of complex molecular interactions using BioNetGen algorithms and the VCell software platform.

Role: PI