

## RECOMMENDATION FOR DR. D. BATTOGTOKH

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Biocomplexity Faculty Search Committee  
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Dear Search Committee:

It is with great pleasure that I write this very strong recommendation for Dr. D. Battogtokh. He has collaborated with me as a postdoctoral fellow in Dr. Berndt Schuttler's theoretical physics group for the last two years on new methods for identifying ensembles of gene regulatory and biochemical reaction networks.

His work is outstanding and very exciting. The **centerpiece of his research effort is a paper published in PNAS USA 99: 16904-16909 (2002) describing a new method of fitting chemical reaction networks involving macromolecules as the participants by an ensemble method used in statistical mechanics.** In this project he developed a simplified reaction network for the *qa* gene cluster in *Neurospora crassa*, one of the two early paradigms for eukaryotic gene regulation (along with the *GAL* cluster). He then proceeded to show that he could identify an ensemble of models consistent with available data on this system.

The key idea is from Boltzman. Faced with many parameters and sparse data, he stepped back from searching for one model that fits the data and instead sought an ensemble of models consistent with the data. This approach resonates with recent work of Alves and Savageau.

Because of his strong biological background he was able to develop for the first time a **formal biological circuit describing the *qa* cluster.** With this model in hand he proceeded to characterize the dynamics of the model by stability analysis as an analytical check on our new fitting procedure for reaction networks.

With a thorough understanding of the kinetics model he then implemented a **novel approach to circuit identification** and was able to recover a circuit that adequately described the *qa* gene cluster when compared with our available profiling data on this system.

I have truly enjoyed this interdisciplinary collaboration with Bat. It has brought in a host of new ideas and opened up an approach to identifying reaction networks, a problem that

is close to intractable. We hold a biweekly seminar entitled "computing life" which draws from Physics, Computer Science, Statistics, Genetics, Botany, and several other disciplines, and the theme of the seminar for the last two years has been what Bat has been working on. He has been a lively participant with many good ideas. What comes out in these seminars is his excellent view on the literature.

He keeps track of alternative approaches to kinetics modeling like the use of Boolean networks recently as an approximation to the full chemical reaction network approach. He points out where we need to apply our new methods on test cases like the Oregonator and Brusselator. He tied his own work into other key theoretical work on the kinetics of the *lac* operon. When the seminar took up recent work on the repressilator, he brought in a recent analysis of the model in the literature. He has many concrete and much appreciated suggestions on improving manuscripts by students in the seminar.

**He is comfortable with the Biology.** He was successful in diving into the molecular biology papers of Norman Giles and Mary Case and extracting the relevant observations to build his model. Understanding the real biology is an earnest desire of this biophysicist!

Then of course he has the mathematical training for the analysis. His **background is broad** in this area, and it shows up in the range of tools he had to bring to bear on the circuit identification problem, from stability analysis and numerical analysis of the resulting differential equations to Monte Carlo methods for fitting these models. All of this work he has implemented on his own. His interest in the area of reaction networks is longstanding, dating back at least to his German advisor. So, he brings a broad perspective to the problems he works on and to others. His experience has benefited computer science students focused on numerical analysis in the computing life seminar and other students focused on modeling other reaction networks like the repressilator.

Dr. Battogtokh's work is highly regarded in the field because he has solved a difficult problem and because he has published over 20 papers in the area of nonlinear dynamics. His work has been presented in seminars in the US, Germany, Russia, and Japan. His work has appeared in very prestigious journals, such as the Proceedings of the National Academy of Sciences and the Handbook of Industrial Mycology, an encyclopedia for fungal biology.

I hope he will continue to work on this circuit identification problem and bring to bear the ensemble method on another very important biological example, the cell cycle, which he has been steeped in his collaboration with Tyson. He has many research opportunities ahead of him because of his strong training and productivity.

**His communication skills are excellent.** He routinely made presentations in the seminar, and they were always excellent. He is engaging. He is a good laboratory citizen. He makes a difference to those around him. He is a good colleague.

**He compares favorably with several previous postdoctoral fellows in my laboratory.**

Dr. Yunxin Fu (now full professor at University of Texas - Houston) had comparable modeling skills but was stronger by training in statistics and produced more papers (4 in his tenure). Dr. Yuhong Wang (now at Merck Bioinformatics) was not as strong as Bat in his training in Monte Carlo Methods nor had his broad perspective on modeling, but was stronger in his biochemical background. Bat has the same level of productivity as a recent postdoctoral fellow Dr. Hemant Kelkar (now Bioinformatics Scientist at University of North Carolina - Chapel Hill), but Bat is much stronger on the mathematical side, while Hemant was much stronger on the biological side. Dr. Budak Arpinar (my most recent postdoctoral fellow, now assistant professor of computer science at UGA) was stronger in producing papers and in his computer science training, but he was far weaker in his biological background than Bat. I have been very fortunate to work with such a talented individual as Bat. Here is my ranking of Bat relative to four other recent postdoctoral fellows in my laboratory:

Table 1. Ranking\* of Dr. Battogtokh with four previous postdoctoral fellows in my lab.

Name	Productivity	Comput. Sci	Statistics	Modeling	Biology
Arpinar	2	1	4	3	5
Battogtokh	4	2	2	1	3
Fu	1	4	1	2	4
Kelkar	5	5	5	5	1
Wang	3	3	3	4	2

\* Postdocs are ranked from high (of 1) to a low (of 5) according to 5 criteria.

**Summary:** Dr. Battogtokh has made a fundamental contribution to the identification of chemical and biological reaction networks. He has also made a fundamental biological contribution by developing a working reaction network for one of the classic paradigms of eukaryotic gene regulation, the *qa* gene cluster. He is successful in communicating his ideas. He has a broad perspective and training on reaction kinetics and nonlinear dynamics, and finally he has an excellent mathematical and biological background (particularly in nonlinear dynamics) to be a strong contributor to your center. I wholeheartedly and without reservation recommend him for a faculty position. Bat is at the heart of where biology is going.

Feel free to call me at (706) 542-1449, if you have any questions.

Yours sincerely,

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