UNIVERSITY OF ILLINOIS
AT URBANA - CHAMPAIGN

Department of Chemical
& Biomolecular Engineering
THE UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

114 Roger Adams Laboratory, Box C-3
600 South Mathews Avenue
Urbana, IL 61801-3602 USA

Richard D. Braatz, Professor and University Scholar
University of Illinois at Urbana-Champaign
Phone: (217) 333-5073
Fax: (217) 333-5052
http://brahms.scs.uiuc.edu
E-mail: braatz@uiuc.edu

Professor Yves Brun
Systems Biology/Microbiology Faculty Search
Department of Biology
Indiana University
Jordan Hall 142
1001 East Third Street
Bloomington, IN 47405-7005

November 17, 2005

Dear Prof. Brun:

Rudiyanto (Rudi) Gunawan receives my highest recommendation for an assistant professor position in your department. Rudi is simultaneously highly intelligent, flexible, creative, thorough, and productive. He is a more productive and capable researcher than any of the ChBE department's PhD graduates over the past 15 years who now hold faculty positions, including at U Minnesota, U Wisconsin, UT Austin, U Pennsylvania, and U Delaware.

I advised Rudi's MS thesis in the area of model reduction and control theory and co-advised his PhD thesis with Prof. Ed Seebauer on the modeling and control of rapid thermal annealing during the manufacture of ultrashallow junctions during CMOS device processing. Rudi joined my research group with a joint BS degree in Chemical Engineering and Mathematics from the University of Wisconsin. His strong background in mathematics became quickly apparent in his courses and research. In his MS thesis Rudi resolved essentially all theoretical and computational issues associated with the control of large scale linear systems with model uncertainties. In a highly independent manner, he thoroughly interrogated the journal papers in the field, located a subtle error in journal papers published by well-known control theorist Charles Desoer in the ECE department at UC Berkeley, wrote theorems and proofs for new results, implemented existing and new numerical algorithms, and thoroughly investigated and resolved all theoretical issues. Rudi's results showed that many accepted model reduction algorithms have key flaws, including extreme sensitivity to small perturbations in the model. His MS thesis which was completed after 2 years was stronger than most PhD theses in control theory.

Having solved the main open control problems that were posed to him during his first year as a graduate student in his MS thesis, Rudi decided to switch areas and do research in semiconductor processing. Prof. Ed Seebauer had approached our group with the problem of constructing a simulation model for boron diffusion in silicon during rapid thermal annealing. Rudi formulated a set of partial differential equations that was significantly more complete and rigorously justifiable than the previous models. Rudi did all of the theory, simulation, and modeling in all of the joint papers with Ed Seebauer. Unlike other simulation models for this process, all of the parameters are rigorously justified and none of the first-principles equations have empirical concentration-dependent diffusion coefficients or other ad hoc tweaking of parameters as used in other models. In addition, a novel process was invented that manipulates chemistry during rapid thermal processing to produce improved transistor junctions, that can extend the lifetime of rapid thermal annealing technologies by a decade. Rudi investigated and verified the idea through simulations first, whose predictions were later verified by experiments. The new process is described in a U.S. patent that is pending.

Rudi was such a productive student that I asked him to contribute to other projects that I wanted driven to completion, although the projects were not directly related to his MS and PhD theses. He wrote a paper which showed that in-situ laser backscattering, ATR-FTIR spectroscopy, and limited use of off-line optical microscopy could be used to identify nucleation and growth kinetic parameters for crystallization processes in which the crystals change shape. Rudi also unofficially advised an MS student while I was away

on sabbatical at MIT. In the first few days of his direct supervision, Rudi identified and resolved several key errors in the student's implementation of a finite volume algorithm that had eluded the student for months. Rudi directed the writing of the student's thesis and an associated software manual, and he published a journal manuscript based on the results. Rudi's graduate results were key in many of the research awards I have received in recent years, including the ASEE Curtis W. McGraw Research Award, the AIChE CAST Outstanding Young Researcher Award, and the IEEE Antonio Ruberti Young Researcher Prize.

Rudi taught a graduate course on open-ended experimental design during Fall 2000. This course covered all of the tasks required to design an optimized process, including experimental design, data analysis, process modeling and simulation, parameter estimation, and optimization. Rudi already had a deep understanding of the background material, so teaching the course that semester did not take too much time from his research. I talked to several students in his class near the end of the semester, and they all gave highly positive reviews on Rudi's performance as an instructor.

Besides being exceeding bright and thorough, Rudi is more flexible and creative in his thinking than any graduate student or postdoctoral fellow whom I have encountered. He moves with ease between deriving theorems in mathematical control theory to implementing a state-of-the-art simulation algorithm to analyzing experimental data from secondary ion mass spectroscopy or laser backscattering.

Rudi has the drive and determination to establish a well-funded research program, and the temperament to excel in all aspects of scholarship. Rudi speaks well and is very sociable and well-liked by his peers. He was one of the most well-liked graduate students in the department. He regularly offered to help other graduate students, and worked perfectly with other graduate students and postdocs in my laboratory. Rudi is a very rare graduate student who is a "complete package"---mathematically strong, able to quickly understand experimental papers outside of his area of expertise, very strong socially, excellent writing skills, and the strong desire to drive research projects to completion without sacrificing completeness or quality. His ability to write proposals describing his research ideas is evident from his selection as a finalist for the Burroughs-Wellcome Career Award at the Scientific Interface, which is based on a bioresearch proposal.

Many researchers in the systems area have "crossed over" into systems biology, including Nikolaos Sahinidis, Costas Maranas, Prodromos Daoutidis, Mike Henson, and Wayne Bequette. Based on my service on a dozen search committees for bioresearch-oriented faculty (including currently serving as the faculty search chair for 2 open positions in the bio area), Rudi is the most promising crossover researcher in systems biology that I have encountered. From another perspective, I would rate Rudi as among the best of all faculty members hired in the U.S. with background in process systems engineering in the past 20 years. Rudi is heads-and-shoulders above all junior process systems faculty hired in the last 10 years, which includes faculty at the University of Wisconsin, UCLA, Rice, Penn State, University of Pittsburgh, University of Toronto, University of Alberta, McMaster University, and Imperial College of London.

Rudi is a natural leader, with strong interpersonal skills, a high degree of professionalism, and will likely become a department head within 10 years of starting a faculty position. His English is better than that of most native English speakers.

It is my opinion that Rudi is the most promising faculty candidate from the U of I Department of Chemical and Biomolecular Engineering in 15 years, including graduates who are currently faculty members at top research universities across the country. If he had not received his Ph.D. from the University of Illinois, I would work very hard to recruit him here. I recommend Rudi in the strongest possible terms.

Sincerely,

Richard Braatz

Richard D. Braatz, University Scholar and Professor of
Chemical and Biomolecular Engineering, Bioengineering,
Mechanical and Industrial Engineering, Applied Mathematics,
and Computational Science and Engineering
Affiliate, Beckman Institute, Molecular and Electronic Nanostructures Area
Affiliate, Center for Nanoscale Science and Technology

UNIVERSITY OF CALIFORNIA, SANTA BARBARA

BERKELEY • DAVIS • IRVINE • LOS ANGELES • MERCED • RIVERSIDE • SAN DIEGO • SAN FRANCISCO

SANTA BARBARA • SANTA CRUZ

DEPARTMENT OF COMPUTER SCIENCE SANTA BARBARA, CALIFORNIA 93106-5110

November 19, 2005

Professor Yves Brun
Systems Biology/Microbiology Faculty Search
Department of Biology
Indiana University
Jordan Hall 142
1001 East Third Street
Bloomington, IN 47405-7005

Dear Professor Brun,

It is a great pleasure to write a letter in support of Dr. Rudiyanto Gunawan for a tenure-track faculty position at your University. I have known Rudi for about two years, during which time he has been a postdoc in my collaborator Frank Doyle's research group.

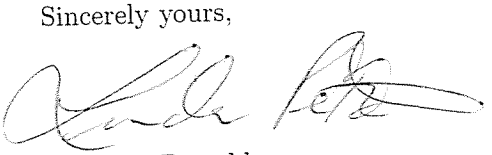
Rudi's work at Santa Barbara has focused on the development of analytical and computational techniques for model development and analysis, in the area of systems biology. Model development and experimental design are two key areas in systems biology where there is a large potential for impact of systems approaches on biological research methododology and results. The problems coming from biology have some very challenging features: there is never enough data, the data almost always involves a large amount of uncertainty, and it is often impossible to obtain data for some parts of the system. In the papers [8,9], Rudi brought to bear in a systematic approach some of the relevant techniques from control theory to model development and experimental design for biochemical systems. Rudi has undoubtedly become an expert in nontraditional sensitivity analysis for the investigation of systems in biology. We worked together with him to develop and employ sensitivity analysis of discrete stochastic models. Sensitivity analysis generally involves computing the derivatives of system outputs with respect to system inputs or parameters. Taking the derivative of a discrete stochastic response is of course not possible. Approximating such a derivative (which doesn't exist) via finite differences yields a large variation of results. What we did in [14] was to focus instead on the derivatives of the probability density functions of the system outputs. The Fischer Information Matrix was used to identify those parameters to which the system is more robust or more fragile. Rudi was the lead author on that paper and a very strong contributor. Around UCSB, Rudi is probably best known for his work on sensitivity analysis of oscillating biochemical systems, in particular for the analysis of Circadian rhythm. He has developed and refined methods for computing the sensitivity of derived quantities such as the period and the phase of the oscillation[20]. He has also been a strong contributor to the Biospice project.

In my opinion, Rudi has been very productive. He is in a great research area with a wealth of important and challenging problems, and is on a strong research trajectory. He is a pleasure to work with and is both an effective leader and a team player.

I have no direct experience with Rudi with respect to classroom teaching, although he is an excellent lecturer and I would expect those skills to carry over into the classroom. He has been a very effective and popular mentor to the graduate students in Frank's group, and has clearly earned their respect. The students go to him for his cogent explanations of concepts in sensitivity analysis, and they come away with a better understanding.

I would recommend Rudi for a tenure-track position in systems biology or chemical engineering in any top Department with no hesitation.

Sincerely yours,



Linda R. Petzold
Professor and Chair, Department of
Computer Science
Professor, Department of Mechanical
& Environmental Engineering

UNIVERSITY OF CALIFORNIA

BERKELEY • DAVIS • IRVINE • LOS ANGELES • MERCED • RIVERSIDE • SAN DIEGO • SAN FRANCISCO

SANTA BARBARA • SANTA CRUZ

Francis J. Doyle III
The Duncan and Suzanne Mellichamp Chair in Process Control

Department of Chemical Engineering
Santa Barbara, CA 93106
(805) 893-8133
(805) 893-4731 FAX
doyle@engineering.ucsb.edu

November 21, 2005

Professor Yves Brun
Systems Biology/Microbiology Faculty Search
Department of Biology
Indiana University
Jordan Hall 142
1001 East Third Street
Bloomington, IN 47405-7005

Dear Yves:

I am writing this letter in support of Rudi Gunawan's application for a faculty position at Indiana. I have been Rudi's supervisor for his postdoctoral research studies here at UCSB since September 2003. **Rudi is clearly the most intelligent, most creative, and most productive postdoctoral fellow that I have known over my professional career of 13 years with affiliations at 4 different universities.**

I have known Rudi for a little over 5 years, as his PhD research at the University of Illinois was in an area of interest to my group. At the time that he applied for a post-doc in my research group, his PhD adviser (Prof. Richard Braatz) ranked him as the best research student that he had supervised in that very competitive program. Rudi's training is in theoretical control, with applications to materials design and particulate problems. These contributions are nicely detailed in his research summary. I recruited Rudi to UCSB to work on problems in systems biology, knowing that his background was mathematics and control theory. In the short time that he has been at UCSB, he has been remarkably successful in mastering the key concepts of molecular biology that are relevant for his project. Furthermore, as demonstrated by several publications to date, he has made inroads in the research area of systems biology.

Rudi is presently working on several projects, and making tremendous strides on multiple fronts. The first assignment that he worked on was a formal method for calculating the sensitivity of stochastic models of biological systems. This required both theoretical developments in the formulation of information theoretic operators for stochastic systems, as well as deep analysis of specific biological problems to determine the relevant classes of systems that would require such analysis. Rudi's work identified biological switches as one important class of problems that required such an approach. **His theoretical analysis of stochastic biological systems, in collaboration with Linda Petzold, have yielded a paper in *Biophysical Journal*,** and the application to a biological switch is underway (in collaboration with Adam Arkin's group), with a publication likely this winter.

A second area that Rudi has been involved is in the formulation of methods for the identification of large scale network models in systems biology. In particular, the problem of iteration between experiment and model development has received little formal analysis, and Rudi (in collaboration with a PhD student in my group) has formulated an algorithm for convergence of this iterative process. The method includes the

optimal determination of a measurement set for a given problem. **An application to a caspase signaling network has been detailed in a manuscript recently submitted to *BMC Bioinformatics.*** Rudi is the lead author of an invited chapter for an upcoming text to be published by MIT Press on *Systems Biology*. The chapter addresses the general problem of network inference, and Rudi's lead authorship reflects his interfacial role in bringing systems engineering tools to problems of model identification in biological networks.

A third area that Rudi has made very nice preliminary contributions is in the robustness analysis of circadian gene networks. Rudi's specific idea is a formal method for computing the phase sensitivity of a nonlinear limit cycle system. In the last 6 months, I have included these preliminary results in talks that I have given to various chronobiology groups, and it is this result which has generated the most interest. Rudi is in the process of refining the theory and expects to apply the results to circadian models in *Drosophila* and mammals, and we have submitted the first manuscript on this work to *Biophys. J.* **I expect Rudi's analyses to have a tremendous impact in the chronobiology community, connecting classical notions of phase relationships in circadian clocks with more current efforts in robustness analysis of biological networks.**

There are several other areas that Rudi has made research contributions towards systems understanding of biological systems. These include a medical problem proposed by collaborators in the Army (Walter Reed Army Institute for Research) for the detection of biothreats using dynamical mathematical modeling and sensitivity analysis. His work has been instrumental in the initial model development as well as the identification of "hot spots" of tremendous sensitivity in the signaling network. This suggests opportunities for optimal vaccine development and administration. He is also mentoring a computer science PhD student in my group on the development of a toolkit for sensitivity analysis of biological systems (BioSens) that is a component of the well known BioSpice project from DARPA.

Rudi has been an excellent mentor for several graduate students, as well as an undergraduate student in my research group during the past 24 months. He is a very effective teacher, and I expect multiple co-authored presentations and publications to come from those mentored projects.

Clearly, in the 24 months that Rudi has been working with me, he has had tremendous productivity. An adviser would be happy with the level of progress that he achieved in any one of these areas, let alone the multiple areas simultaneously. I can honestly that of the approximately 30 graduate students and 10 postdoctoral fellows with whom I have worked over the past 13 years at the University of Delaware, Purdue, Stuttgart, and UCSB, **Rudi is clearly the most intelligent, most independent, and most productive**. I would rank him significantly above the junior faculty that I know at these institutions, as well as junior faculty in chemical engineering and bioengineering at other top 10 departments in the US (Berkeley, MIT, Princeton, etc.). I expect that he will be tremendously successful as an academic.

I offer my strongest and unreserved endorsement of Rudi Gunawan as a candidate for a faculty position at Indiana. His training in traditional mathematics and control theory and his initial postdoctoral research success in systems biology problems make him an ideal faculty candidate.

Sincerely,

Francis J. Doyle III
Professor