Guelph,
December 8, 2005,

Professor Yves Brun
Systems Biology Faculty Search,
Department of Biology
Indiana University
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Subject: Cover letter by Dr. Arni SR Srinivasa Rao

Dear Chair,

I am very much interested to apply for the faculty position that your department advertised.

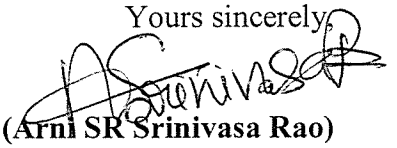
Currently I am working as a postdoctoral fellow in the Department of Mathematics and Statistics, **University of Guelph**, Canada. I will be moving to the **University of Oxford**, UK for one year academic visiting position from 1 February 2006. Prior to coming to Canada, I was working as a fellow in the Young Scientist Scheme for Mathematical Sciences, funded by the Department of Science and Technology, New Delhi. This was an independent position and I was based at **Indian Institute of Science**, Bangalore

I do research in mathematical biology, probability theory and biostatistics. For instance I have worked on applying mathematics to the biology, epidemiology and immunology of HIV to establish the relations between important variables and to estimate the parameters are of present research activities. My theoretical work is on convergence principles in general and those in probability functions applicable to epidemiology in particular. I have been studying the functional convergence of certain continuous functions, CLTs and branching processes. I have 12 publications (including those in press) and a few more submitted.

I will be very happy to take up faculty position in the US to continue my work in above mentioned areas and I look forward to a productive career in inter-disciplinary research activities. I have very serious interest to teach and interact with students and I am very confident about it. I have a very satisfactory teaching score in 2005.

I will be very happy to furnish any further information you require in support of my application. Please find enclosed a detailed CV with publication list, my research statement, and my teaching statement. I look forward to hearing from you.
Thank you very much.

With best regards,
Yours sincerely,



(Arni SR Srinivasa Rao)

Postdoctoral Fellow
University of Guelph, Canada

Research Statement of Dr. Arni SR Srinivasa Rao

Mathematics Subject Classifications: 92 (primary), 60 (secondary).

My research is in mathematical biology in general and mathematical and stochastic epidemiology in particular.

My interests and achievements in mathematical biology have resulted in collaborations and frequent discussions with a number of internationally reputed people in the field, viz, Professors Roy Anderson, Herbert Hethcote, Philip Maini, Vidya Nanjundiah and Lord Robert May. Currently I am working as a postdoctoral fellow under the supervision of Professor Chris Bauch, University of Guelph, Canada. With him I am developing and analysing SEIR models for Hepatitis A virus (HAV) in Canada and to obtain theoretical results for the probability of extinction of HAV. I will be moving to the University of Oxford to take one year academic visiting position from 1 February, 2006 to work with Professor Philip K Maini.

Entry into mathematical biology and recent past research

My interests in population biology began during the early days of my PhD dissertation (1996-97), when I started to work on Lotka's integral equations for a stable population model [1] and subsequently on Preston's famous work on destabilized populations [2]. Although I have written couple of papers published in regional journals, those were not part of my dissertation because I wanted to carry out more practical applications of mathematics and statistics to population biology problems of current interest. I choose to work on HIV/AIDS models in 1997 and interacted frequently with medical doctors in Bombay to understand AIDS data problems and their expectations from a mathematician. At that time I did not see any publication on HIV modeling work from researchers in India and that led me to frame the objective for my PhD to develop ODE models and methods based on convolution approaches. Understanding the fundamental ideas on modeling of AIDS [3], mathematics of infectious diseases [4] and techniques required for biomathematics [5] were very helpful at various stages of my early career.

AIDS epidemiology was not easy at that time: I had worked with public health experts and clinicians to understand AIDS epidemiology in India. I suggested a model based method to estimate AIDS related mortality in Bombay (The Lancet, 1999) [10]. These results were highlighted as a news article in the popular newspaper *Times of India*. This study established for the first time that there were thousands of deaths due to AIDS in Bombay in the mid-90s. Subsequently, I presented a model based approach as a working group member to UNAIDS, to initiate a large scale study. This model was also cited by several researchers in the field. During this period, I was also involved in several studies relating to incidence and prevalence. However these studies were not published due to the insufficient sample size of the available data.

Rigorous mathematical methods: During the third year of my PhD, (1999), I have been working on more mathematical problems and comparatively less on empirical and data related models. During the period 1999 - 2004 I worked at two prestigious research Institutes in India and University of Oxford. Exposure in these Institutes stood as foundation for my mathematical career. First, at Indian Statistical Institute (as a Visiting Scientist) I collaborated extensively on parametric models, and ODEs for the epidemiology of AIDS and second at Indian Institute of Science (as a young scientist fellowship holder under mathematical sciences) I worked on AIDS mathematical modeling and teaching mathematics and statistics. There was a big step in my research career in mathematical biology when I visited to the Centre for Mathematical Biology (Oxford) for several months and Imperial College School of Medicine (London) in 2002-03. During 2002-03, I twice served as a consultant for the World Bank to develop models for key issues related to AIDS.

My present collaborators (Alphabetically)

Mathematics subject classifications: 92A15, 92C60, 62P10, 92D30.

1. **Professor Chris T Bauch**, University of Guelph (one manuscript to be submitted [6], two manuscripts in progress [7, 8])

Area: Hepatitis A Virus epidemiology, extinction probabilities. Summary: We have formulated an age structured SEIR model and incorporated a new compartment of vaccinated individuals, which turned our model into an agestructured SEIRV model. Our objective is to formulate a policy framework to distribute

vaccines in Canada. We have added dynamics related to travelers who bring the virus into Canada. Thus our model fundamentally differs from earlier SEIR models in terms of the dynamics of its various compartments. We have provided model based optimum vaccine policy options for HAV in Canada, estimated R_0, and forces of infection for Canadian population. The immediate application of our model is to obtain cost effective analysis, which is being carried out in collaboration with public health experts in Canada.

We have proved results that provide extinction probability for the Hepatitis A in general under theoretical setup. We have constructed a branching process $\{Z_n\}$ for size of the infected population in the n^{th} generation. Our results are based on dynamics of mean number of infection for the entire process. We will eventually write a more practical paper based on these results that estimates probability of extinction in Canada.

2. **Professor Geoff P Garnett**, Imperial College, London (one manuscript [9]).

Area: HIV Virus dynamics. Summary: Several models have been published describing the within human dynamics of HIV and the changes in the HIV population associated with treatment. In this survey, we describe their initial development to the stage where a set of generic consensus model underpin much theoretical research in this area. The majority of the models have similar assumptions on the dynamics of uninfected, infected cells and virus and were successful in explaining immunological data. However it is still possible to further develop presently available models to improve their ability in assessing drug efficacy and understanding its infection kinetics.

3. **Professor Masayuki Kakehashi**, Hiroshima University (two papers published [10], one in press [11] and one in progress [12]).

Area: HIV epidemiology. Summary: Analysis of the Indian AIDS data was carried out for various sub group populations. Time between HIV infection and development of AIDS is called the incubation period of AIDS. We have developed our own deconvolution method to estimate incubation period. This method works as follows: Suppose we know HIV infection density and AIDS density, then incubation period distribution is deconvoluted from the other two functions. This method worked well when hospital based data on incubation period is not available. We applied successfully this method to estimate the truncated as well as non-truncated incubation period. Our third joint work was on general ODE mathematical models in infectious diseases prediction. In this we have discussed various methods and gave examples from Japan and Indian infectious diseases scenario.

We are currently working on models that estimate individual drug efficacy and parameter estimation.

4. **Professor Philip K Maini**, University of Oxford (one manuscript [9], one in progress [12]).

Area: HIV epidemiology, AIDS drug dynamics, HIV virus dynamics. Summary: A detailed survey on HIV virus dynamics models was conducted and potential areas of improvement in the earlier models were illustrated with theoretical examples.

We reconstructed earlier ODE models for AIDS epidemiology and converted them into integro-differential equations to analyze the impact of drug therapy as follows. Instead of assuming a constant $1/d$ (average incubation period), we assume it varies based on the drug type. Thus we define, $1/d_i = \int_{\mathbb{R}} z_i dG(z_i)$, (Stieltjes integral) for $i = 0, 1, 2, 3$, where $i = 0$ stands for without drug scenario, $i = 1$ for *drug1*, $i = 2$ for *drug2* and $1 = 3$ for *drug3*. Here G is the probability density function with certain parameter set $\mathcal{B}$ and z_i is a continuous random variable representing the incubation period. Here z_i is a real valued function defined on probability space $(\Im, \mathbb{A}, P)$, where $\mathbb{A}$ is a Borel field, $\Im$ is space of elementary events and $P(\mathbb{A})$ is probability of the event $A \in \mathbb{A}$. We demonstrated parameter estimation procedure for modified model and performed stability analysis.

My independent research[10, 13, 14]

Mathematics subject classifications: 60J85, 92D30.

Apart from my collaborative research, I have my own specific research activity and objectives. I have been trying to prove that probabilistic limit theorems can be utilized for long term understanding of epidemic spread. This type of analysis is new to the mathematical biology community. Reporting of a given disease plays a crucial role is assessing the spread in the population. When each disease case is reported more than once, then we say multiple reporting exists in the population. If (Ω_n) and (Λ_n) represent sequences of reported and total number of cases, then $\Lambda_n \in \mathcal{B}_\epsilon(\Omega_n)$ under certain conditions. Here $\mathcal{B}_\epsilon(\Omega_n)$ is the

$\epsilon-$neighborhood of Ω_n. When multiple reporting is present then $\Lambda_n \in \mathcal{B}_\epsilon(K_n - \eta_n)$, n^{th} reporting class and n^{th} empty class. A set of limit theorems were proved and a recent work incorporates realistic situation to prove further results. These works includes not only the efficiency of reporting as a difference of reported and total, but also impact of multiple reporting. The results presented here are original and brings a new outlook to study epidemic behavior in a probabilistic way.

In the past I have developed a methodology for computing probability of extinction of HIV in the presence of protease inhibitors. This methodology was based on branching process principles. I have provided some computations based on published data from HIBV immunology.

Using the next generation operator approach and traditional methods, estimation of basic reproductive rates in an ODE model is also a focus of research.

Research motto and future plans

I am open to collaborating on research problems in ecology, immunology and environment. In addition to these, I intend to continue my interactions with government and non-governmental agencies in epidemic and disease modeling and research consultancy.

I wish to continue both my theoretical and applied research. I have long term goals of integrating probability theory and mathematical biology and help to answer questions frequently arise in data limitations, parameter estimation for ODE models. Some of my ongoing collaboration introduces these issues. I have frameworks to develop limit theorem approaches suitable for epidemiology analysis.

Grant applications

I have been thinking on grant proposals based on my research motto described above. I have been also in touch with some key people from prestigious funding agencies like NSF etc and also winners of big grants. Upon getting a tenure-track position I will apply for grants. My academic positions or residence status from the past couple years did not permit me to apply for the same.

References

[1] Lotka, Alfred J. (1942). Ann. Math. Statistics 13, 115–126.

[2] Preston, SH and Lahiri, S. (1991). Math. Pop. Stud., 3 (1), 39-51.

[3] Anderson RM, May RM (1988). Nature 333 (6173): 514-519.

[4] Hethcote, HW. The mathematics of infectious diseases. SIAM Rev. 42 (2000), no. 4, 599–653.

[5] Murray, JD. (1993) Mathematical biology. Second edition. Springer-Verlag, Berlin.

[6] **Rao A.S.R.S**. Bauch CT, et al. An Age Structured SEIRV type model for Hepatitis A in Canada (to be submitted).

[7] **Rao A.S.R.S**. Bauch CT Probability of extinction of HAV in Canada. (in preparation)

[8] Bauch CT, Tricco, Ba P, **Rao A.S.R.S,** Gilca V, Duval B and Murry K. Outbreak pattern and dynamic transmission of Hepatitis A in a low endemicity country (in preparation).

[9] **Rao A.S.R.S**, Garnett G.P and Maini P.K Mathematical models for HIV viral dynamics and drug efficacy. (completed, yet to be submitted).

[10] See my CV for refereed published/inpress list (7 - single authored, 4 lead authored and 1 - co-authored).

[11] Kakehashi, M and **Rao, A.S.R.S**. Mathematical and statistical approaches to risk management for the prevention of HIV/AIDS and other infectious diseases. (in press)

[12] **Rao A.S.R.S**., Kakehashi M and Maini PK On estimation of varying incubation periods for a dynamical model. (in preparation).

[13] **Rao A.S.R.S.** On estimation of R_0 in age structured SEIRV model (technical report-2005)

[14] **Rao A.S.R.S.** Limit theorem approach in epidemic reporting analysis (submitted).

Teaching Philosophy of Dr. Arni SR Srinivasa Rao

Since the beginning of my pre-high school days to graduate courses in various cities in India, I have come across some really good teachers and also some not-so-impressive teachers. I have learned the art of impressive teaching from several very good teachers. The common mistakes committed by some not-so-impressive teachers also helped me to plan my teaching style by avoiding those mistakes. Some of the excellent teachers inspired me to pursue my career in probability and mathematics very seriously.

Summary

My limited teaching activities in Canada have been successful. I believe that whenever possible, one should integrate their research with their teaching to give context and relevance to the mathematics being taught. This will greatly enhance the learning environment, give me the opportunity to share my enthusiasm and excitement about the discipline, and motivate my students to further studies in mathematics. Here is an idea about my experience and philosophy as a teacher.

Early teaching foundation

I used to teach my juniors and classmates on topics in undergraduate mathematics, statistics and physics. Then this teaching became more organized during my master's degree. Especially, I started enjoying to help my classmates just few days before exams on how to link various topics such that it is easy to remember the sequence of topics in the syllabus. At that time there were other classmates who were also helpful to fellow classmates. My pet subjects for which friends liked to interact and learn from me were (beginning from UG to PhD courses): differential equations, distribution theory, real analysis, linear algebra, special functions, modern physics, operations research, probability theory I & II, design of experiments (combinatorics part), demography, biostatistics (survival analysis part). Most of these informal teaching cum interaction experience helped me enormously when I started to teach formal courses at Indian Institute of Science, Bangalore. The teaching style of statement - proof and how to approach a given problem in mathematics by **Professor M. Perisastri** [1] during my UG days is still a strength for me. He was also genius in college mathematics and published several papers in pure mathematics. His broad knowledge in history of mathematics taught in India and England used to motivate many of the students for decades. His style played important role in my thought process till I finished PhD. Then during my tenure at Indian Statistical Institute, Calcutta I met great teacher **Professor BV Rao** [2], who has influenced my teaching such that my students get maximum benefit from me. I owe a lot to these two teachers in India before I started to teach in North America.

Teaching experience in Canada

Professor Chris T Bauch [3] **and Professor Joe Cunsolo** [4] acted as teaching mentors for me to help to adjust to the North American teaching requirements like student-teacher interactions, student's expectations from the instructor and other necessary suggestions during my teaching in the University of Guelph. It helped me to get the **Overall score for effectiveness as a teacher: 3.9 on a scale of (1 - 5)** for the summer 2005 course - Introductory Calculus I. In addition to this, I was a participant at the New Researcher's Conference -2005 organized by the Institute of Mathematical Statistics (IMS). Here we were mentored by some experts of college teaching in the USA. I believe these exposures are a positive addition to my maturing as an effective teacher.

MATH 1050 (Winter 2005) Mathematical Modeling (problem sessions only), University of Guelph: I taught about ten sessions. The main course was taught by Professor Bauch, who mentored me on basics of teaching in Guelph. The topics covered were linear programming, simplex method, introductory matrix algebra, probability and population dynamics. This exposure molded me to teaching in Canada. I did not get any official feedback about my teaching, however a few students who were weak in solving problems said they felt better after my supplementary sessions. That time my only strategy was to help the students as much as I could and make them comfortable in solving assignment problems. I tried my best to help them and I am glad that some of them did feel that they benefited out of it.

MATH1000DE (Summer 2005) Introductory Calculus I, University of Guelph: I was Instructor for this course. This is an on line course for first year UG students. Students interacted on line with me and some students met in person to learn more. I have completely enjoyed teaching this course. The average time that I spent with students and prepare my subject content was three hours (except during attending conferences outside the country). I took two weeks initially to understand the depth, motivation and natural interest of students for this course, and then I would cluster students into different categories. Usually students kept me busy by asking questions on assignments and general questions on concepts. So my clustering of students assisted me to help a particular student based on his/her prior knowledge level. By the end of first assignment, I was almost sure of most of their interests and motivation levels.

In addition to their questions and clarifications, I always kept them very busy by uploading points on the beauty of calculus and on chapter highlights. I made them realize how important it is to master analytical and imaginative ideas of calculus.

Three out of five assignments that I gave were tough. I observed that students interact within one another more if any assignment is tough. Any question still unanswered among the students used to be followed by me regularly and I used to give them hints on that. Importantly, those students who scored more than 70 percent in the first assignment, continued to be very good for all subsequent assignments and the final exam. Ten out of thirty three students who were not good at the beginning improved by the end of fifth assignment.

Experience in India

Probability 2002-03 & 2003-04 (1/3rd of course on mathematics and statistics) (Indian Institute of Science):

Students: Integrated PhD students in Biological Sciences and engineering divisions. I started formal teaching at Indian Institute of Science, Bangalore during the academic year 2002-03. The students of probability were first year integrated PhD students (who come after finishing their pre university course, called B.Sc) and almost all have same background at their pre-university level. I know that I needed a special preparation to teach such students, as the competition to get admission into IISc is very intense. Usually a maximum of 12 students are selected from across the country. My strategy for them was as follows: I like to introduce the course and give a general idea of what the topic is about in the first class. I also explain the history behind it and try to determine what the students may already know about the topic. I develop a friendly atmosphere so they ask as many questions as possible. I also conduct surprise tests, particularly early in the course so that students do not procrastinate. As the course progresses, I come back to the topics already covered and try to get answers and clues from students to prove the current theorem or to establish a concept. This helped me to somewhat assess their capacity for understanding and (or) also my teaching abilities regarding that particular derivation or concept. Especially for probability I found this kind of teaching plan worked well. Eventually students understood what probability is about and what its real life applications are. I would suggest several problems and invite them to meet me over coffee/tea to discuss them. I mix with students very well and make efforts to be accessible. In developing my teaching skills,

Introduction to Mathematical Biology 2003-04 (Indian Institute of Science):

Students: PhD and Masters of Engineering students with Mathematics background. My teaching philosophy for mathematical biology was different from that for probability. My students in this course were engineering and mathematics graduate students. Engineering stream students are enrolled only if they have already done a course on introductory differential equations and learned some analysis concepts. Though I introduced the topic and other things as above in the probability course, I gave them several exercises to model a given phenomenon in biological science I checked the model they constructed and then I offered improvements. I included my own experiences and those of my colleagues on dealing with real data and building a model. In case of bad fits or unavailability of the data, I discussed how best we can construct a model in light of these limitations. This (I assume) gave students a semi-realistic exposure to the field problems a mathematician has to deal with. My time at the Centre for Mathematical Biology, Mathematical Institute, Oxford inspired me to teach this course. This course generated good interest in the students as well in faculty at the Indian

Institute of Science; I think it was the first time such a course was officially offered. I have received positive feedback from students and faculty, in the form of emails, for introducing this course. Six out of eight students gave a personal assessment of very good or excellent and two gave an assessment of average.

Teaching Motto and Future plans

I am willing to teach basic courses as well as advanced courses. My strategy for effective teaching and learning is thorough preparation, seeding the concepts clearly, motivating the students to spend sufficient time on the course at home/library and developing a friendly atmosphere.

References

[1] Popular college level teacher and musician. Published also on Fermat's last theorem including in Math. Asoc. America journals & Crelle's journals during 1950s and 1960s.
[2] Highly respected teacher and mentor to many. Published also on set theory and probability including in Am. Math. Soc. journals.
[3] Highly published researcher in mathematical biology.
[4] Won several teaching awards including the Canada national 3M teaching Fellow award for teaching at the university level.

Some comments on me by my students

" I have really been enjoying the course, and you have been a wonderful professor. I am actually taking 3 on line courses this summer, and you are the only prof that responds to emails so quickly, and constantly communicates with the students on the conferences. This is very helpful! So thanks for making the course enjoyable, Good luck in your future courses as a professor :) " by Magdalena Adamczenko

"I would like to thank you for making this a really great learning experience for us all. I know I got a lot out of this course. All the best to you in the future!" by Madiha Rana

"Our instructor was very quick and clear with answering all questions. I felt that he was very approachable and had a genuine interest in us as students. Thank you for a great course" by Anonymous