

Modelling infectious diseases*

The mainstream mathematical modelling community in India has, by and large, remained aloof from the problems of infectious disease modelling. This is in contrast to the situation in many other countries where inter-disciplinary teams, which incorporate epidemiologists, applied mathematicians, statisticians, statistical physicists, clinicians and veterinary scientists, work together in studying infectious disease propagation. In the UK, such collaborations have yielded rapid response strategies to address the spread of foot-and-mouth disease and avian influenza, with such strategies typically implemented within weeks of the first reported case. Connecting the clinical and public health community with the modelling community assumes special significance for India in the light of newly reported virulent multi-drug-resistant strains of TB, the possibility of a SARS pandemic, recent outbreaks of chikungunya and dengue as well as other diseases which affect large numbers of the Indian population, such as malaria and tuberculosis.

The recent workshop on 'Modelling Infectious Diseases' held at the Institute of Mathematical Sciences (IMSc), Chennai attempted to bridge this gap by putting together biologists, clinicians and public health specialists working on infectious diseases with scientists from a modelling background. This meeting had its genesis in a meeting on systems biology held at Manesar earlier this year, where infectious disease modelling was one of the several themes discussed. The Institute of Mathematical Sciences (IMSc) workshop was planned mainly as an open-ended interaction between the two communities. Its other purpose was to see if current ideas in complex systems research, network analysis and agent-based modelling might be useful in understanding aspects of the spread of infectious diseases. Many of the modelers had little or no prior experience in

modelling infectious diseases, but had considerable expertise in a variety of other areas, ranging from network structure to the statistical description of large data sets. The biologists and clinicians came from a variety of backgrounds, ranging from cell biology to immunology, biostatistics, and public health.

B. Ravindran (Institute of Life Sciences, Bhubaneswar) described the hygiene hypothesis, according to which parasitic organisms inside humans play an important role in shaping immune response, in particular by modulating autoimmunity and allergy. This hypothesis concludes, somewhat controversially, that the increasingly hygienic lifestyle of modern humans has led to a higher incidence of non-infectious disorders such as allergy and autoimmunity. This interaction between parasite and human immune response is a challenging question in the field today and a prime candidate for modelling attempts. Vineeta Bal (National Institute of Immunology, Delhi) spoke on the relative lack of success stories regarding vaccines for infectious diseases. Successful vaccines should elicit a long lasting, protective response from the host immune system. However, there are multiple reasons for vaccine failure, including immunological or genetic ones and the complex life cycles of parasites. Vaccines may also not succeed because of public health-related reasons such as the unavailability of vaccine, absence of proper storage or lack of manpower resulting in poor vaccination coverage.

The intra-cellular signalling machinery involved in cellular response to Leishmania infection was described in a talk by Bhaskar Saha (National Center for Cell Science, Pune). Several theoretical groups have worked on modelling the genesis of primary and secondary response in the immune response over the past few decades. Debashish Chowdhury (IIT Kanpur) reviewed his own work on this topic, describing both discrete and continuum approaches. Host-pathogen interactions also change over evolutionary time-scales, a topic explored in the talk of Aparup Das (National Institute of Malaria Research, Delhi) on the genome evolution of the malaria parasite.

While these talks explored infection at the micro-level, other talks examined infection from the macroscopic perspective of how infection spreads through society. Somdatta Sinha (Centre for Cellular and Molecular Biology, Hyderabad) presented an analysis of the spatiotemporal patterns of malaria incidence in India over the past few decades. The problems of reliability and availability of data were discussed in the talk, as these turn out to be major complicating factors in understanding how a particular infection spreads. Interestingly, even data obtained at such low spatial resolution (district-wise incidence) and low temporal resolution (annual incidence) showed evidence of wave-like spreads and sudden spikes in the prevalence. The talk presented approaches at understanding such patterns through the use of spatially detailed models of epidemic spreading. Mohan D. Gupte (National Institute of Epidemiology, Chennai) described models of leprosy used for suggesting remedial measures in the field, also discussing briefly public health aspects of the recent chikungunya epidemic. Other work done at NIE in the context of AIDS and leprosy modelling, was discussed by Vasna Joshua and A. Elangovan.

Mathematical approaches to disease spreading are largely based on the Susceptible-Infected-Recovered (SIR) or Susceptible-Infected-Susceptible (SIS) models. Sunita Gakkhar (IIT Roorkee) explored the effect of immunization on disease spreading through such models. S. S. Manna (S.N. Bose National Centre for Basic Sciences, Kolkata) and Parongama Sen (Calcutta University, Kolkata) both spoke about infection spreading on complex networks, a subject of great recent interest. The SIR and SIS models assume that contacts leading to possible infection occur between randomly assigned individuals. In such models populations are 'well-mixed', so that the probability of any one individual being infected is only proportional to the fraction of infected individuals in the populations. In reality, social contacts rarely occur in such random fashion: we are far more likely to know people who are mutually acquainted with each other. This

*A report on Modelling Infectious Diseases – a workshop sponsored by the IMSc Complex Systems Project and held during 4–6 September 2006 at Chennai. More details are available from http://www.imsc.res.in/past_conf.html

implies that the contact network is highly 'clustered', in the language of network theory. In addition, a few 'long-range' connections can occur between individuals with no mutual acquaintances. Real societies also contain individuals who have contacts with far more people than the average, as for example, people who work in various service industries. Such 'hubs' of contact networks are obviously far more important in spreading infections than a typical member of such a network. Recent ideas concerning disease propagation on such complex networks suggest that the identification and selective immunization of such hubs might be a more effective and efficient strategy of containing infections than vaccination strategies aimed at an entire population.

A study of spreading on networks applied to computer networks was reported in the talk of Niloy Ganguly (IIT Kharagpur). Sudeshna Sinha (IMSc, Chennai) spoke about a cellular automata-based model of epidemic that also implemented similar complex network connections. The related class of excitable media models were shown to reproduce many observed spatial and temporal patterns of epidemics in the talk by Sitabhra Sinha (IMSc, Chennai). In particular, these models explore how infections may apparently disappear and come back after a significant interval of time. Gautam

Menon (IMSc, Chennai) briefly introduced the basic ideas of agent-based computational models to simulate the actual spread of infections in geographically and community-wise structured urban settings.

The spreading of infectious diseases can be modelled at many levels of description, ranging from the single cell to the tissue, organism and society. Modellers distill, from this complexity, those components which admit a mathematical or computational description. An important component of the meeting was discussion sessions aimed at identifying the questions which could be addressed by modelling. Much was clarified in these discussions and we summarize their conclusions here: Micro-level and macro-level phenomena cannot be strictly compartmentalized, even though the principles governing the modelling may differ superficially. Biologists tend to see the underlying complexity in predicting infectious disease progression and may not necessarily make the distinction between what is less important and what is more important in terms of abstracting to simple models. In contrast, modellers tend to simplify matters first and then to construct models in which such simplifying assumptions are built in from the start. There is thus a need for continued interaction between these communities to reconcile these very diverse approaches;

until a common language is developed, understood and assimilated by the interacting partners, fruitful collaborations are unlikely to emerge.

The other point made was that modellers require access to data to evaluate model predictions and make suggestions for data acquisition, but often have no idea where such data might be available. Data sharing requires, typically, a formalized arrangement between those who collect clinical and epidemiological data and users of such data, but the general feeling at the meeting was that negotiating such access for academic purposes would not be a problem. Material which relates to such data, describing the type of data available and listing persons who may be contacted in this regard, will be placed on the meeting website. Those interested in establishing contact with a broader set of scientists and applied mathematicians interested in the problems of infectious disease modelling are urged to write to the conveners of this meeting.

Gautam I. Menon* and **Sitabhra Sinha**, The Institute of Mathematical Sciences, Chennai 600 113, India; **Vineeta Bal**, National Institute of Immunology, Delhi 110 067, India; **Somdatta Sinha**, Centre for Cellular and Molecular Biology, Hyderabad 500 007, India.

*e-mail: menon@imsc.res.in

MEETING REPORT

Biological control of insect pests and diseases of forestry importance*

E. Meru, Rain Forest Research Institute (RFRI) in his presidential remarks said that the seminar was a platform for the scientists to discuss and exchange their ideas and knowledge about the importance of biological control, use of botanicals, genetic engineering, etc. A. K. Pathak, Director of Research, AAU, Jorhat inaugurating the seminar stated that there was

a great need to intensify research on biological control because indiscriminate use of chemical pesticides have polluted the environment to such an extent that the biodiversity of the region has been threatened to extinction. They get accumulated in the food chain thereby causing great harm to human health.

L. K. Hazarika, Entomology Department, AAU, in his keynote address, highlighted various insect pests of forestry importance, their damage potential, and available natural enemies against those insect pests. He emphasized that the biological control approach is the only suitable method for forest insect pest

management. An invited lecture was delivered by B. G. Unni, RRL, Jorhat and he described the plant based bio-control against various insect pests and diseases and listed their biochemical and functional properties very briefly.

In the lead lecture of the first technical session, B. K. Borthakur of Tocklai Experimental Station, Jorhat described the prospects of biocontrol of tea diseases in northeast India. He stated that due to continuous application of pesticides, many pests and pathogens in tea plantations become resistant to them. To overcome this, efforts must be made to isolate and identify some indigenous bio-control agents.

*A report of the seminar on Recent Trends in Biological Control of Insect Pests and Diseases of Forestry Importance sponsored by Department of Science and Technology, New Delhi, held on 18 September 2006 at Rain Forest Research Institute, Jorhat.