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Abstracts of Invited and Contributed Talks & List of Posters

Detecting and quantifying between-pathogen interactions in humans: an agent based model simulation study

Hélène Arduin, Laurence Watier, Didier Guillemot, Lulla Opatowski
Unité B2PHI, UMR 1181 Inserm – Université de Versailles Saint Quentin en Yvelines - Institut Pasteur

Abstract

Population models of pathogen transmission generally focus on a single pathogen. However, growing evidence suggest that microorganisms interact within the host [1]. These interactions may impact the global dynamics of a pathogen and lead single-pathogen-studies to erroneous conclusions.

Interaction studies are commonly performed by applying regression methods (Linear, Poisson and negative binomial) [2] as well as dynamic models fitting on disease incidence data [3]. To what extent are these methods reliable in this context? Here we present a simulation study in which we assess the ability of these different methods to achieve detection of between-pathogen associations.

We used an agent-based-model to simulate the co-circulation of two pathogens in a human population. Specifically, influenza viruses and pneumococcus were modelled as influenza effects on pneumococcus have been documented in humans [4]. To explore a range of hypotheses, three interaction parameters were defined: synergy in pneumococcus-acquisition, -transmission, and –infection [5]. By varying these parameters 38 scenarios of interactions were simulated, from which weekly influenza and pneumococcal infection incidence time series were extrapolated.

Each statistical method was independently tested on these simulated datasets, and methods results were compared on their ability to detect and quantify the force of association. All methods were roughly able to detect strong interaction links. However for intermediate and low interactions, regressions did not always return significant associations, there was a threshold of detection varying with the interaction hypothesis: at least a

4-times increased probability for pneumococcus-transmission and –acquisition was needed to detect a significant association, whereas a 6-times increased probability of pneumococcus infection was necessary. Furthermore, the time lags at which significant associations were detected strongly depended on the interaction hypothesis: detected over the 6 preceding weeks for pneumococcus-acquisition, over the 7 preceding weeks for pneumococcus-transmission, and only over the 3 preceding weeks for pneumococcus-infection.

This study highlights that assessing between-pathogens interactions from time series incidences is possible, although careful methodological selection is needed. Better knowledge of existing interactions is needed as it could offer new possibilities for treatment and control of major diseases.

Bibliography

[1] Short, K., & Habets, M. (2012). Interactions between Streptococcus pneumoniae and influenza virus: a mutually beneficial relationship? Future Microbiology, 609–624.

[2] Nicoli, E. J., Trotter, C. L., Turner, K. M. E., Colijn, C., Waight, P., & Miller, E. (2013). Influenza and RSV make a modest contribution to invasive pneumococcal disease incidence in the UK. The Journal of Infection, 66(6), 512–20.

[3] Opatowski, L., Varon, E., Dupont, C., Temime, L., van der Werf, S., Gutmann, L., Boëlle, P., Watier, L. & Guillemot, D. (2013). Assessing pneumococcal meningitis association with viral respiratory infections and antibiotics: insights from statistical and mathematical models. Proceedings. Biological Sciences / The Royal Society, 280(1764), 20130519.

[4] Weinberger, D. M., Harboe, Z. B., Viboud, C., Krause, T. G., Miller, M., Mølbak, K., & Konradsen, H. B. (2013). Pneumococcal disease seasonality: incidence, severity, and the role of influenza activity. The European Respiratory Journal, 1–19.

[5] McCullers, J. A. (2006). Insights into the interaction between influenza virus and pneumococcus. Clinical Microbiology Reviews, 19(3), 571–82.

Fast and accurate estimation of field effectiveness for meningococcal vaccines through dynamic modeling.

Lorenzo Argante(1,2,3), Michele Tizzoni(2), Duccio Medini(2,3)

1. PhD School in Complex Systems for Life Sciences, University of Turin, Turin, Italy.

2. ISI Foundation, Turin, Italy.

3. GSK Vaccines, Siena, Italy.

Abstract

Estimating the field effectiveness of a recently introduced vaccine such as Bexsero is fundamental to monitor the impact of immunization programs. The screening method has been widely used, and is proposed for a post-implementation study in UK, as it provides an estimate of effectiveness based only on number of disease cases and vaccine coverage.

However, the precision of the screening method is proportional to the number of disease cases detected. If the incidence of the disease is low, as for MenB in general and in UK particularly over the last three years, several years are required to obtain a relevant estimate of vaccine effectiveness.

Here, we propose a Monte Carlo maximum likelihood (MCML) procedure for estimating the vaccine effectiveness via a dynamic computational model. Based on the most relevant features of the epidemiology of the pathogen and on the social contact pattern of the host population, a dynamic transmission model realistically reproduces both the spreading of the pathogen and the emergence of disease cases. A maximum likelihood method is
then used to compare the stochastically generated cases with the real ones, leading to an estimate of the most credible vaccine effectiveness.

The MCML method was validated against data collected during the MenC vaccination campaign carried out in UK between 1999 and 2008. An accurate

and precise estimate of vaccine effectiveness against disease could be obtained in a significantly shorter time frame, compared to the screening method. The MCML procedure also provided a reliable estimate of vaccine effectiveness against carriage, not obtainable through the screening method, in line with the *herd immunity *effect previously measured in this vaccination campaign.

Projections to the Bexsero immunization program in UK indicate that months would be sufficient to estimate vaccine effectiveness with MCML, providing a precious tool for fast and accurate post-implementation surveillance.

Bibliography-

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002333/human_med_001614.jsp&mid=WC0b01ac058001d124

- Trotter, Caroline L., Nigel J. Gay, and W. John Edmunds. "Dynamic models of meningococcal carriage, disease, and the impact of serogroup C conjugate vaccination." *American Journal of Epidemiology* 162.1 (2005): 89-100.

- Campbell, Helen, et al. "Updated postlicensure surveillance of the meningococcal C conjugate vaccine in England and Wales: effectiveness, validation of serological correlates of protection, and modeling predictions of the duration of herd immunity." *Clinical and Vaccine Immunology* 17.5 (2010): 840-847.

- Ionides, E. L., C. Bretó, and A. A. King. "Inference for nonlinear dynamical systems." *Proceedings of the National Academy of Sciences* 103.49 (2006): 18438-18443.

Global analysis of an infection age model with a class of nonlinear incidence rates

Bentout Souflane and Touaouala Tarik Mohamed

Department of Mathematics, University Abou Bekr Balkaid, Tlemcen, Algeria

Abstract

SIR infection age models with a very general class of nonlinear incidence rates $f(S,J)$ are investigated. We give a necessary and sufficient condition for global asymptotic stability of the free-equilibrium related to the basic reproduction number.

Furthermore, additional conditions allow us to prove an exponential stability of this disease-free equilibrium. Finally, by using a Lyapunov functional, we show the global asymptotic stability of the endemic equilibrium whenever it exists.

Bibliography

Hal L. Smith, Horst R. Thieme, Dynamical Systems and Population Persistence, Graduate Studies in Mathematics V. 118, AMS, 2011.

P. Magal, C.C. McCluskey, G.F. Webb, Lyapunov functional and global asymptotic stability for an infection-age model. Applicable Anal, 89, No 7, 2010, 1109-1140.

A. Korobeinikov, Lyapunov functions and global stability for SIR and SIRS epidemiological models with non-linear transmission. Bull Math Biol, 68, 2006, 615-626

Optimal Varicella immunization programs for both Varicella and Herpes Zoster Control

Monica Betta 1, Marco Laurino 2, Andrea Pugliese 3, Giorgio Guzzetta 4, Alberto Landi 1, Piero Manfredi 5

1 Department of Information Engineering (DIE), University of Pisa, Italy.

2 Institute of Life Science, Scuola Superiore Sant'Anna, Pisa, Italy.

3 Department of Mathematics, University of Trento, Italy.

4 Bruno Kessler Foundation, Trento, Italy.

5 Department of Statistics and Mathematics Applied to Economics, University of Pisa,Italy.

Abstract:

A main obstacle to the widespread adoption of varicella immunization in Europe has been the fear of a subsequent boom in natural herpes zoster caused by the decline in the protective effect of natural immunity boosting due to reduced virus circulation. We apply optimal control to simple models for VZV transmission and reactivation to investigate existence and feasibility of temporal paths of varicella childhood immunization that are optimal in controlling both varicella and zoster. We analyze the optimality system numerically focusing on the role played by the structure of the cost functional, the relative cost zoster-varicella, and the length of the planning horizon. We show that optimal programs exist but will mostly be unfeasible in real public health contexts due to their complex temporal profiles. This complexity is the consequence of the intrinsically antagonistic nature of varicella immunization programs when aimed to control both varicella and herpes zoster. However we could show that gradually increasing, smooth – thereby feasible - vaccination schedules, can perform largely better than routine programs with constant vaccine uptake. Moreover we show the optimal temporal profiles of feasible immunization

programs targeting with priority the mitigation of the post-immunization natural zoster boom.

Bibliography:

[1] Nardone, A. et al. 2007 The comparative sero-epidemiology of varicella zoster virus in 11 countries in the European region. Vaccine 25, 7866–72. (doi:10.1016/j.vaccine.2007.07.036)
[2] Hope-Simpson, R. E. 1965 The nature of herpes zoster: a long-term study and a new hypothesis. Proc. R. Soc. Med. 58, 9–20.
[3] Oxman, M. N. 2009 Herpes zoster pathogenesis and cell-mediated immunity and immunosenescence. J. Am. Osteopath. Assoc. 109.
[4] Brisson, M., Gay, N. J., Edmunds, W. J. & Andrews, N. J. 2002 Exposure to varicella boosts immunity to herpes-zoster: implications for mass vaccination against chickenpox. Vaccine 20, 2500–2507. (doi:10.1016/S0264-410X(02)00180-9)
[5] Schuette, M. 1999 Modeling the Effects of Varicella Vaccination Programs on the Incidence of Chickenpox and Shingles. Bull. Math. Biol. 61, 1031–1064. (doi:10.1006/bulm.1999.0126)
[6] Guzzetta, G., Poletti, P., Del Fava, E., Ajelli, M., Scalia Tomba, G. P., Merler, S. & Manfredi, P. 2013 Hope-Simpson's progressive immunity hypothesis as a possible explanation for herpes zoster incidence data. Am. J. Epidemiol. 177, 1134–42. (doi:10.1093/aje/kws370)
[7] Poletti, P. et al. 2013 Perspectives on the impact of varicella immunization on herpes zoster. A model-based evaluation from three European countries. PLoS One 8, e60732. (doi:10.1371/journal.pone.0060732)
[8] Comba, M., Martorano-Raimundo, S. & Venturino, E. 2012 A Cost-Effectiveness-Assessing Model of Vaccination for Varicella and Zoster. Math. Model. Nat. Phenom. 7, 62–77. (doi:10.1051/mmnp/20127306)

Statistical challenges when analysing emerging epidemic outbreaks

Tom Britton

Stockholm University

Abstract

New infectious disease outbreaks have great impact on communities over the world as most recently manifested by the Ebola outbreak. An important statistical task is then to predict the future scenario with and with out preventive measures. In the current talk we will investigate such analyses and see how it can be improved. The main catch is that in the exponentially growing phase early on in an outbreak, several biases can occur if not taken into account for: events with short delays will be over-represented. We will give some examples from the Ebola outbreak and see how the biases can be removed or at least reduced. (Joint work with Gianpaolo Scalia Tomba).

Gaussian process approximations of the stochastic SIR model.

Elizabeth Buckingham-Jeffery, University of Warwick.

Thomas House, University of Manchester.

Abstract

Syndromic surveillance is used to enhance traditional disease surveillance methods. The collection of syndromic data often requires less direct manual input and has lower associated costs. Therefore the data can be collected at more frequent time intervals and is often available more immediately. Computational speed of analysis methods is important when working with syndromic data as new data is available so frequently.

The stochastic SIR model is used to model epidemics of infectious diseases. One benefit of a stochastic model over a deterministic one is that some variability in the expected behaviour of the epidemic can be seen. It is beneficial to know the potential extent of this variability when using the model to make predictions about an epidemic. However the stochastic SIR model is non-linear, therefore analytical measures of its variability are not possible.

The aim of this work is to approximate the variability in the epidemic trajectories of the stochastic SIR model using a Gaussian process approximation [1]. We compare Gaussian process approximations with different means and standard deviations to numerical simulations of the stochastic SIR model using the Kullback-Leibler divergence. We use the multi-variate normal moment closure approximation as a comparison benchmark [2].

We find that for large population sizes the optimal Gaussian process approximation works equally as well as the established multi-variate normal moment closure approach. The optimal time-varying normal approximation is computationally faster. Finding a good Gaussian process approximation enhances the possibilities for real-time analysis of syndromic disease data.

Bibliography

[1] C. Archambeau, D. Cornford, M. Opper, and J. Shawe-taylor. Gaussian Process Approximations of Stochastic Differential Equations. Journal of Machine Learning Research: Workshop and Conference Proceedings, 1:1-16, 2007.

[2] V. Isham. Assessing the Variability of Stochastic Epidemics. Mathematical biosciences, 107(2):209 - 224, 1991.

Qualitative analysis and optimal control of deterministic epidemic models including information–related human behavior

Bruno Buonomo

Department of Mathematics and Applications, University of Naples Federico II

via Cintia, I-80126 Naples, Italy.

email: buonomo@unina.it

Abstract

Over the last few years, there have been significant developments in the field of mathematical theory of the spread of infectious diseases. These developments concerns the role of the feedback enacted onto an epidemics by the available information and rumors on the propagation of the infectious spreading itself.

This new viewpoint substantially changed the nature of models in mathematical epidemiology. Indeed, its classical models adopt an approach derived from statistical physics and theoretical chemistry: subjects are represented as interacting particles, so that the infection process, for example, is modeled by means of the mass–action of chemistry [1, 7, 10].

In this talk, we will focus on epidemic models including information–related human behavior. We present several results contained in recent papers [2, 3, 4, 6] and obtained in the framework of the new field of Behavioral Epidemiology [8, 9].

Bibliography

[1] Anderson R. M., May R. M., Infectious Diseases of Humans. Dynamics and Control, Oxford University Press, Oxford, 1991

[2] B. Buonomo, d'Onofrio A., Lacitignola D., Global stability of an SIR epidemic model with information dependent vaccination, Math. Biosci., 216, 9–16 (2008)

[3] B. Buonomo, d'Onofrio A., Lacitignola D., Rational exemption to vaccination for non-fatal SISdiseases: globally stable and oscillatory endemicity, Math. Biosci. Engin., 7, 561–578 (2010)

[4] B. Buonomo, d'Onofrio A., Lacitignola D., Globally stable endemicity for infectious diseases with information-related changes in contact patterns, Appl. Math. Letters, 25, 1056–1060 (2012)

[5] B. Buonomo, d'Onofrio A., Lacitignola D., Modeling of pseudo-rational exemption to vaccination for SEIR diseases., J. Math. Anal. Appl., 404, 385-398 (2013)

[6] B. Buonomo, d'Onofrio A., Manfredi P., Optimal balancing of the interplay of public intervention and private choices to minimize the cost of vaccination programmes, In preparation.

[7] Capasso V., Mathematical Structures of Epidemic Systems, Lecture Notes in Biomathematics, Springer-Verlag, Berlin, 2008

[8] d'Onofrio A., Manfredi P., Salinelli E., Vaccinating behaviour, information, and the dynamics of SIR vaccine preventable diseases, Theor. Pop. Biol. 71 (2007) 301–317.

[9] Manfredi P., d'Onofrio A. (eds), Modeling the Interplay Between Human Behavior and the Spread of Infectious Diseases. Springer (2013).

[10] Murray J. D., Mathematical Biology, Springer, 2002

The interplay between models and public health policies: Regional control for a class of spatially structured epidemics (*think globally, act locally*)

Vincenzo Capasso

ADAMSS (Interdisciplinary Centre for Advanced Applied Mathematical and Statistical Sciences)

Universitá degli Studi di Milano

Milan, Italy

Abstract

A review of the research carried out by the speaker on the mathematical analysis of epidemic systems. Particular attention will be paid to recent analysis of optimal control problems related to spatially structured epidemics mediated by environmental pollution.

A relevant problem, related to the possible eradication of the epidemic, is the so called zero stabilization. In a series of papers, necessary conditions, and sufficient conditions of stabilizability have been obtained. It has been proved that it is possible to diminish exponentially the

epidemic process, in the whole habitat, just by reducing the concentration of the pollutant in a nonempty and sufficiently large subset of the spatial domain. The stabilizability with a feedback control of harvesting type is related to the magnitude of the principal eigenvalue of a certain operator. The problem of finding the optimal position (by translation) of the support of the feedback stabilizing control in order to minimize both the infected population and the pollutant at a certain finite time.

Is intervention a cost-effective way to increase vaccination coverage? A real option approach

Zuzana Chladná, Department of Applied Mathematics and Statistics, FMFI, Comenius University, Bratislava, Slovakia, e-mail:chladna@fmph.uniba.sk

Abstract:

Current measles outbreaks in USA and Germany emphasize the importance of sustaining and increasing vaccination coverage rates in case of vaccine preventable diseases. In Slovakia, despite mandatory vaccination scheme, decrease in the vaccination coverage against measles has been observed in recent years. Intervention at the country level appearsto be the only strategy to help improve thevaccination coverage rate and thus achieve herd immunity.

This study aims to analyze the economic effect of intervention in Slovakia. We develop a real options model given uncertainties in vaccination coverage and epidemics outbreak appearance.Vaccination coverage is represented as a stochastic process and intervention as a one-period jump of this process. Using real options techniques we determine the level of vaccination coverage at which it is optimal to perform intervention.We compare the epidemic-related economic costs with and without intervention. A detailed sensitivity analysis of numerical results shows the main factors, whichaffect economic efficiency of intervention.

Bibliography:

Chladná Z., Moltchanova E.: Incentive to vaccinate: A synthesis of two approaches.To appear in Acta Mathematica Universitatis Comenianae.

Shefer A., Briss P., Rodewald L. et al. Improving immunization coverage rates: an evidence-based review of the literature.Epidemiological Reviews1999; 21(1): 96-142.

Dixit, A.K., R.S. Pindyck (1994), Investment under Uncertainty, Princeton University Press, Princeton, N.J.

Modelling age-dependent population dynamics of Anopheles gambiae s.s., taking into account the effect of environmental temperature during the immature and mature stages

Céline Christiansen-Jucht, Imperial College London, London, United Kingdom;
María-Gloria Basáñez, Imperial College London, London, United Kingdom;
Kamil Erguler, Energy, Environment, and Water Research Center, The Cyprus Institute, Cyprus;
Adam Saddler, Swiss Tropical and Public Health Institute, Basel, Switzerland;
Jacob Koella, Université de Neuchâtel, Neuchâtel, Switzerland;
Paul Parham, University of Liverpool, London, United Kingdom

Abstract

Climate change and global warming are emerging as important threats to human health, particularly through the potential increase in vector- and water-borne diseases. Environmental variables are known to affect significantly the population dynamics and abundance of insect disease vectors, but the exact extent and consequences of this sensitivity are not yet well-established. We focus here on malaria and its main mosquito vector in Africa, Anopheles gambiae s.s., and present a set of novel mathematical models of climate-driven mosquito population dynamics based on the results of laboratory research into the effects of senescence and temperature during its immature and mature stages on mosquito survival and reproduction life-history parameters. We use the results of experimental work to inform the structure of mathematical models of age- and temperature-dependent Anopheles population dynamics, and compare the fit of these models to 'standard' models that ignore temperature- and age-dependence. We observe that when compared with models that do not include temperature- and age-dependence, these models demonstrated a significantly better fit to longitudinal datasets of vector abundance in sub-Saharan Africa. This highlights that including both temperature- and age-dependence in the vector component of mosquito-borne disease models is important for more reliably predicting disease transmission dynamics, particularly in relation to the potential effects of global warming

Ebola epidemic growth, transmission patterns, and insights for epidemic control

Gerardo Chowell-Puente

Georgia State University, Atlanta, USA

Abstract

The 2013-15 Ebola epidemic in West Africa has provided a unique opportunity to increase our understanding of the transmission dynamics and control of Ebola virus disease. In this presentation i will talk about several studies that we have conducted during the course of the Ebola epidemic and aimed to: 1) characterize the local and regional epidemic growth patterns, 2) assess the role of spatial dynamics using simple models to gain insights for epidemic control, and 3) quantify Ebola transmission patterns by systematically analyzing Internet news reports from authoritative media outlets and public health authorities in order to overcome the scarce and patchy information on exposure patterns and chains of transmission available from formal epidemiological surveillance efforts.

Modelling rabies elimination in an African city

Nakul Chitnis

Swiss Tropical and Public Health Institute

Basel, Switzerland

Abstract

Rabies is a viral disease that is usually transmitted by the bite of an animal. While rabies in wildlife has been eliminated in Western Europe through oral vaccination of foxes, dog transmitted rabies persists in Asia and Africa. Most human deaths from rabies occur in tropical, resource limited countries, where an estimated 55,000 people die of rabies each year (usually contracted through dog bites). We ran two vaccination campaigns in N'Djamena, Chad in 2012 and 2013, reaching a coverage of 70% of dogs and eliminating rabies transmission. Concurrently, we calibrated an existing compartmental ordinary differential equation model of transmission of rabies in dogs. We analysed this model to elucidate the reasons for the loss of immunity and determine the threshold density of susceptible dogs required to maintain transmission and the optimal frequency of vaccination campaigns.

MCMC Methods applied to epidemic outbreaks

Valentina Clamer & Andrea Pugliese

University of Trento, italy

Abstract:

The attention that was given to the A/H1N1 2009 flu pandemic has made it possible to collect detailed data on the epidemic spread in more typical contexts, especially schools that are well known to represent hot spots for epidemic spread. Data on infection during that pandemic were collected also among students of two primary schools in Trento (Italy). Although the data obtained were not detailed (and possibly not accurate), we show how their analysis yields estimates of transmission rates within class, grade or school, that appear consistent between the two schools and with our general understanding.

Since the data are only partially observable (information is not available on all students; furthermore, only dates of symptom occurrence, not of infection, are known), the by now classical approach of Markov Chain Monte Carlo Methods is followed to make inference about the missing data and the unknown parameters. Before applying the algorithm to actual data, we applied it to synthetic data, generated to reproduce the school structure, under different assumptions on the structure of infection transmission. This work on synthetic data makes us, on the one hand, get a better interpretation of the results obtained, showing for instance to which degree parameters are identifiable, on the other hand, assess the loss in accuracy resulting from missing data and other sources of error.

Bibliography:

-Philip D. O'Neill A tutorial introduction to Bayesian inference for stochastic epidemic models using Markov chain Monte Carlo methods, Mathematical Biosciences 180 (2002) 103-114
-S. Cauchemez, A. Bhattarai, T.L. Marchbanks, R.P. Fagan, S. Ostroff, N.M. Ferguson, D. Swerdlow anda the Pennsylvania H1N1 working group Role of social networks in shaping disease transmission during a community outbreak of 2009 H1N1 pandemic infuenza, PNAS, vol. 108, no.7 2825-2830
-W.R. Gilks, S. Richardoson and D.J. Spiegelhalter Markov Chain Monte Carlo in practice, Chapman & Hall/CRC, 1996

Facing the complexity of infectious disease spread: the MERS case

Vittoria Colizza

INSERM & UPMC, Paris, France

Abstract

The Middle East respiratory syndrome coronavirus (MERS) that causes a severe lower respiratory tract infection in humans is considered a serious public health epidemic threat. Since its isolation in June 2012, MERS has reached 26 countries infecting a total of 1,368 confirmed cases, with approximately 40% mortality (WHO Summary Update, July 7, 2015). The majority of cases has occurred in the Middle East region, where the disease is endemic, with cases being reported in other countries in Europe, North America and Asia in people who travelled from the Middle East or their contacts. MERS cases have displayed variations in time and across geography affecting the generation of cases along the zoonotic and human-to-human transmission routes, thus increasing the complexity of the epidemic spread and challenging our understanding of the situation. Here I will present an integrative analysis based on epidemic data in the Middle East and cases exported out of the region to assess the transmission scenario in the endemic region during the initial phase of the outbreak and evaluate its changes in time and space. The combined modeling approach is based on a spatial-transmission model integrating mobility data worldwide and allows for variations in the zoonotic/environmental transmission and under-ascertainment. It synthesizes evidence from multiple sources of information: sizes of clusters of cases, traffic data, time-series of case incidence in the region and imported cases outside the region. The methods used account for the limited information available and reporting inaccuracies. Our findings provide important information aiming at a more comprehensive understanding of MERS-CoV circulation in the Middle East region.

On the mechanisms for persistence of the rabies virus (RABV): effects of spatial fragmented population and incubation period heterogeneity

D. Colombi

Computational Epidemiology Laboratory, Institute for Scientific Interchange (ISI), Torino, Italy

Dipartimento di Fisica, Università degli Studi di Torino, Italy

C. Poletto

INSERM, UMR-S 1136, Institut Pierre Louis d'Epidemiologie et de Sante Publique, F-75013, Paris, France

Sorbonne Universites, UPMC Univ Paris 06, UMR-S 1136, Institut Pierre Louis d'Epidemiologie et Sante Publique, F-75013, Paris, France

H. Bourhy

Institut Pasteur, Unit lyssavirus dynamics and host adaptation, Paris, France

V. Colizza

INSERM, UMR-S 1136, Institut Pierre Louis d'Epidemiologie et de Sante Publique, F-75013, Paris, France

Sorbonne Universites, UPMC Univ Paris 06, UMR-S 1136, Institut Pierre Louis d'Epidemiologie et Sante Publique, F-75013, Paris,France

Institute for Scientific Interchange (ISI), Torino, Italy

Abstract

Rabies is a fatal zoonosis caused by the RABV virus and characterized by a complex epidemiological situation which remains a serious public health problem in developing countries. Rabies incidence is largely attributed to the growth of domestic dog population which is the most important vector for the human exposure. Phylogenetic and virological analysis of isolates collected in Bangui, the capital city of the Central African Republic, indicate the presence of several sequentially circulating subtypes and a value of the reproductive number R0 close to one. None of this subtypes seems to be maintained in the canine population in the sole population of Bangui and mechanisms underlying the virus persistence are still unknown.

Two main factors may be at play: the spatial fragmentation of the host population, that may favor the importation of isolates from outside the city, and unusually heterogeneous incubation period of the disease (median close to one month and a range from 10 days to more than one year). To study the specific role and interplay of these two factors on the RABV epidemiology in this region, we introduced a stochastic metapopulation epidemic model, where the dog patches and corresponding populations are obtained from human demographic data and geography, and known dogs-to-humans ratios in urban and rural settings. We tested two frameworks – namely, the exponential framework, where the incubation and infection periods are exponentially distributed (as in basic compartmental models), and the realistic framework where we consider realistic distributions for incubation and infectious periods. Exploring a range of epidemic scenarios, we found that the virus is not able to persist in the canine population in the exponential framework for values of the reproductive number R0 smaller than 1.16. Realistic distributions of the incubation period would instead favor persistence, allowing the virus to circulate even for lower transmissibility (R0 = 1.05), compatible with the observed situation.

Bibliography

[1] Hawthorne L Beyer, Katie Hampson, Tiziana Lembo, Sarah Cleaveland, Magai Kaare, and Daniel T Haydon. The implications of metapopulation dynamics on the design of vaccination campaigns. Vaccine, 30(6):1014–1022, 2012.

[2] K Brunker, K Hampson, DL Horton, and R Biek. Integrating the landscape epidemiology and genetics of rna viruses: rabies in domestic dogs as a model. Parasitology, 139(14):1899–1913, 2012.

[3] Katie Hampson, Jonathan Dushoff, Sarah Cleaveland, Daniel T Haydon, Magai Kaare, Craig Packer, and Andy Dobson. Transmission dynamics and prospects for the elimination of canine rabies. PLoS biology, 7(3):e1000053, 2009.

[4] Matt J Keeling and Pejman Rohani. Modeling infectious diseases in humans and animals. Princeton University Press, 2008.

[7] Darryn L Knobel, Sarah Cleaveland, Paul G Coleman, Eric M F`evre, Martin I Meltzer, M Elizabeth G Miranda, Alexandra Shaw, Jakob Zinsstag, and Francois-Xavier Meslin. Re-evaluating the burden of rabies in Africa and asia. Bulletin of the World health Organization, 83(5):360–368, 2005.

[8] Tiziana Lembo, Katie Hampson, Magai T Kaare, Eblate Ernest, Darryn Knobel, Rudovick R Kazwala, Daniel T Haydon, and Sarah Cleaveland. The feasibility of canine rabies elimination in africa: dispelling doubts with data. PLoS neglected tropical diseases, 4(2):e626, 2010.

[9] Alun L Lloyd. Destabilization of epidemic models with the inclusion of realistic distributions of infectious periods. Proceedings of the Royal Society of London. Series B: Biological Sciences, 268(1470):985–993, 2001.

[10] Alun L Lloyd. Realistic distributions of infectious periods in epidemic models: changing patterns of persistence and dynamics. Theoretical population biology, 60(1):59–71, 2001.

[11] Chiraz Talbi, Philippe Lemey, Marc A Suchard, Elbia Abdelatif, Mehdi Elharrak, Nourlil Jalal, Abdellah Faouzi, Juan E Echevarŕıa, Sonia Vazquez Moron, Andrew Rambaut, et al. Phylodynamics and human-mediated dispersal of a zoonotic virus. PLoS pathogens, 6(10):e1001166, 2010.

Statistical Modeling of Family Formation Behaviors and Their Impact on HIV in Sub-Saharan Africa

Emanuele Del Fava, Carlo F. Dondena Centre for Research on Social Dynamics and Public Policy, Bocconi University, Milan, Italy

Raffaella Piccarreta, Dept. Decision Sciences & Carlo F. Dondena Centre for Research on Social Dynamics and Public Policy, Bocconi University, Milan, Italy

Simon Gregson, Dept. Infectious Disease Epidemiology, Imperial College London, UK & Biomedical Research and Training Institute, Harare, Zimbabwe

Alessia Melegaro, Dept. Policy Analysis and Public Management & Carlo F. Dondena Centre for Research on Social Dynamics and Public Policy, Bocconi University, Milan, Italy

Abstract

There is an ongoing debate over the possible explanations for the great variation in the size of the HIV epidemic all over sub-Saharan Africa. In particular, it is still unclear which are the consequences of people's choices regarding the ordering and the timing of their family formation events, such as sexual debut, marriage, and parenthood, on HIV risk. Despite the impact of the single family formation events on HIV has been already investigated by the demographic literature (Hallett et al. 2007; Bongaarts 2007; Sandøy et al. 2007), very little work has been done on the relationship between the whole family formation trajectory and the HIV status. There is increasing support towards the idea that health is indeed the result of a continuous process that develops over an individual's lifetime (Macmillan 2005), and that personal decisions on, for example, marriage are necessarily connected to decisions on sexual debut and/or childbearing. Following an approach typical of this "life course epidemiology" (Kuh et al. 2003), we investigate the association between several experienced trajectories of family formation events and HIV risk, while accounting for different socio-demographic factors, timing life course events, and sexual risk behavior factors (number of premarital sexual partners). We use individual data from a longitudinal general population cohort study (spanning 2000 to 2011)

from the Manicaland province of Zimbabwe (Gregson et al. 2006), an area characterized by high HIV prevalence. Our findings are of high relevance for public policies, as it emerges that people whose trajectories show parenthood outside of marriage, and delayed, or never experienced, marriage and parenthood are more at risk for HIV infection than people whose trajectory include all the three events in a short time window.

Bibliography

Bongaarts, J. (2007). Late marriage and the HIV epidemic in Sub-Saharan Africa. Popul Stud, 61(1): 73–83.

Gregson, S., Garnett, G. P., et al. (2006). HIV decline associated with behavior change in Eastern Zimbabwe. Science, 311(5761): 664–666.

Hallett, T., Lewis, J.J.C., et al. (2007). Age at first sex and HIV infection in rural Zimbabwe. Stud Fam Plann, 38(1): 1–10.

Kuh, D., Ben-Shlomo, Y., et al. (2003). Life course epidemiology. J Epidemiol Community Health, 57: 778–783.

Macmillan, R. (2005). The Structure of the Life Course: Classic Issues and Current Controversies. In R. Macmillan (Ed.) The Structure of the Life Course: Standardized? Individualized? Differentiated? 3-24. London: Elsevier.

Sandøy, I.F., Michelo, C., et al. (2007). Associations between sexual behaviour change in young people and decline in HIV prevalence in Zambia. BMC Public Health, 7(1): 60.

Assessing the impact of school closure on the spread of influenza: a data-driven approach.

Giancarlo De Luca (corresponding author)

INSERM, UMR-S 1136, Institut Pierre Louis d'Epidémiologie et de Santé Publique, France,

Sorbonne Universités, UPMC Univ. Paris 6, UMR-S 1136, Institut Pierre Louis d'Epidémiologie et de Santé Publique, France

Kim Van Kerckhove:

Interuniversitary Institute for Biostatistics and statistical Bioinformatics, Hasselt University, Belgium

Chiara Poletto:

INSERM, UMR-S 1136, Institut Pierre Louis d'Epidémiologie et de Santé Publique, France,

Sorbonne Universités, UPMC Univ. Paris 6, UMR-S 1136, Institut Pierre Louis d'Epidémiologie et de Santé Publique, France

Niel Hens:

Interuniversitary Institute for Biostatistics and statistical Bioinformatics, Hasselt University, Belgium

Centre for Health Economics Research & Modeling of Infectious Diseases, Vaccine and Infectious Disease Institute, University of Antwerp, Belgium

Vittoria Colizza:

INSERM, UMR-S 1136, Institut Pierre Louis d'Epidémiologie et de Santé Publique, France,

Sorbonne Universités, UPMC Univ. Paris 6, UMR-S 1136, Institut Pierre Louis d'Epidémiologie et de Santé Publique, France

Abstract

Children are known to fuel the onset of an influenza epidemic owing to the structure of their social contact patterns. During holidays and weekends children's social contacts and mobility are strongly reduced: it is thus expected that these variations affect the spread of influenza epidemics. The amplitude of such effects, however, is still under debate.

In this work, we build an age-structured spatial meta-population model and study the effects of periods of school closure (holidays and week-ends) on the spread of an influenza epidemic. We focus, in particular, on Belgium because of the size of the system and the access the fundamental data for the model development.

We divide Belgium into spatial patches (in our case we use the smallest administrative unit municipality) and within each patch we use a stochastic SEIR compartmental model to describe the spread of the disease. We use an explicit age structure with two age-classes: 0–19 yrs and 19+ yrs. The interaction between classes is described by a set of contact rate matrices representing the contact rates between individuals of different classes during a regular week, a regular weekend, a scholar holiday week and a scholar holiday weekend, respectively. As a consequence the in-patch basic reproduction number R0i of each patch varies in time. Moreover owing to the demographic variations among the patches, Roi changes spatially.

The coupling between different patches is given by the mobility of the individuals. In the case of Belgium only regular mobility is taken into account, since there is no internal air traffic (IATA 2013 data) and it is difficult to quantify non-regular mobility form other sources.

We use mobility data obtained from Belgium 2001, since 2011 mobility data is not yet fully available to infer the structure of the mobility network for Belgium. Since 2001 Belgium Census does not have age-structured fluxes, we infer that structure from 1999 French Census and validate the structure using the displacement information collected as part of a Flemish social contact survey conducted in 2010. We estimate the reduction in commuting during Weekends and holidays using a displacement survey experiment form French Ministry of environment ("Enquête nationale transports et déplacements" 2008) and validate it through data coming from annual job surveys of INSEE.

We firstly investigate theoretically the behaviour of the system for the spread of influenza. We assume a latency period of $1/\varepsilon = 1.1$ days and an infectious period of $1/\mu = 3$ days. We vary the per-contact exposure rate b to analyse the response of the system. We show that the greatest contribution comes from including holidays and weekends induced variations in contact rates. Variations in commuting patterns, instead, only produce a marginal effect at these scales.

We thereafter proceed to validate these results comparing them with the Belgian ILI incidence surveillance data in 2008. To do so we first fit the model to reproduce the ILI incidence data on an arrondissement (the one of Bruxelles) and compare the output of the simulations with the data. Since the ILI data are very noisy we compare only peak times and we find that our model is able to predict the peak time in the majority of the arrondissements with on week uncertainty.

We also find that holidays slow down the epidemic but do not affect epidemic size significantly. We finally proceed to analyse the effect of initial conditions and the impact of latency, and we find that the effect of holidays is maximal when they occur after the initial phase of the epidemic but before the peak is reached.

Boosting and waning : on the dynamics of immune status

Odo Diekmann , Utrecht University

Abstract

The aim is to describe the distribution of immune status (in a stationary population with demographic turnover) on the basis of a within-host sub-model [1] for continuous waning and occasional boosting. Inspired by both Feller's fundamental work [2] and the more recent delay equation formulation of physiologically structured populations [3], we derive, for a given force of infection, a linear renewal equation that can be solved by successive approximation, i.e., by generation expansion (with the generation number corresponding to the number of times an individual became infected).

In joint work in progress with Wilfred de Graaf and Mirjam Kretzschmar we use the generation expansion as a starting point for the efficient computation of coarse statistics.

Bibliography

[1] W.F. de Graaf, M.E.E. Kretzschmar, P.M.F. Teunis, O. Diekmann. A two-phase within host model for immune response and its application to seriological profiles of pertussis. Epidemics (2014) 9 : 1-7

[2] W. Feller. An introduction to probability theory and its applications, Vol. II, Chapter X, Section 3 (Wiley, second edition, 1971)

[3] O. Diekmann, M. Gyllenberg, J.A.J. Metz, S. Nakaoka, A.M. de Roos. Daphnia revisited : local stability and bifurcation theory for physiologically structured population models explained by way of an example. Journal of Mathematical Biology (2010) 61 : 277-318

Transmission dynamics and final epidemic size of Ebola Virus Disease outbreaks with varying interventions

Maria Vittoria Barbarossa 1, Attila Dénes 1, Gábor Kiss 1, Yukihiko Nakata 2, Gergely Röst 1, Zsolt Vizi 1
1 Bolyai Institute, University of Szeged, Szeged, Hungary
2 Graduate School of Mathematical Sciences, University of Tokyo, Tokyo, Japan

Abstract

The 2014 Ebola Virus Disease (EVD) outbreak in West Africa was the largest and longest ever reported since the first identification of this disease. We propose a compartmental model for EVD dynamics, including virus transmission in the community, at hospitals, and at funerals. Using time-dependent parameters, we incorporate the increasing intensity of intervention efforts. Fitting the system to the early phase of the 2014 West Africa Ebola outbreak, we estimate the basic reproduction number as 1.44. We derive a final size relation which allows us to forecast the total number of cases during the outbreak when effective interventions are in place. Our model predictions show that, as long as cases are reported in any country, intervention strategies cannot be dismissed. Since the main driver in the current slowdown of the epidemic is not the depletion of susceptibles, future waves of infection might be possible, if control measures or population behavior are relaxed.

Bibliography

Chowell G, Nishiura H, Transmission dynamics and control of Ebola Virus Disease (EVD): a review. BMC Medicine, 12(1) (2014),196.
Legrand J, Grais RF, Boelle PY, Valleron AJ, Flahault A, Understanding the dynamics of Ebola epidemics. Epidemiol Infect. 135(4) (2007), 610–621.

Optimal control for Epidemiology: choice of cost and introduction of constraints

Filipa N. Nogueira and Maria do Rosario de Pinho

Faculdade de Engenharia da Universidade do Porto
Porto, Portugal
e.mail: mrpinho@fe.up.pt

Optimal Control problems are a powerful tool to test and study different vaccination schedules and treatment of infectious diseases. Numerical and analytical methods of optimal control allow us to simulate different scenarios and confront public policies to control the spreading of infectious diseases. Considering SEIR models for a generic diseases we discuss different choices of cost and the introduction of non-standard constraints in optimal control problems involving SEIR model. We illustrate all our discussion with various numerical simulations.

We take the opportunity to discuss special features of the software used.

Human behaviour: a challenge in modelling epidemic spread

Alberto d'Onofrio
International Prevention Research Institute

Lyon (France)
e-mail: alberto.donofrio@i-pri.org
Joint work with: *P. Manfredi*

Abstract

Classical models of infectious diseases were based on statistical mechanics (SM).

On the one hand classical tools of SM such as the mass-action law were heavy used in the first part of the life of mathematical epidemiology; on the other newer tools of SM, such as network theory, scale-free distributions etc. . . were adopted in recent years.

However, all these approach fails to describe some scenarios because they abstract, in the first case, subjects as particles in random motion, in the second modelling scenario, as networks static or with autonomous changes. In reality human beings are complex active entities endowed by behaviours that impact on the disease spread. In turn, the behaviour is influenced by the available information on the epidemic spread. As a consequence epidemics feedback onto themselves passing through human behaviour. These considerations, expressed in various forms, led to the birth of a new discipline named behavioural epidemiology of communicable diseases (BE). Here we first briefly show some outstanding evidences of the relevance of these issues by means of examples taken from recent history and statistics. Then, we will review our personal contribution, by focusing on some issues concerning the modelling of changes in vaccine propensity and on mathematizing the intervention of public health authorities, and how to use in innovative way SM in BE.

Bibliography

P Manfredi and A d'Onofrio (Eds.) Modeling the Interplay Between Human Behavior and the Spread of Infectious Diseases. Springer (2013)

A d'Onofrio and P. Manfredi. Bistability in a Simple Behavioral Epidemiology Model. Submitted (2015)

Mathematical modeling of pertussis transmission: evaluating the impact of delayed vaccination in infants.

G.Fabricius*(*), P.Pesco(*), P.Bergero(*) and D. Hozbor(**)

(*) Instituto de Investigaciones Fisicoquímicas Teóricas y Aplicadas, Facultad de Ciencias Exactas, Universidad Nacional de La Plata y CONICET, CC 16, Suc. 4, 1900 La Plata, Argentina.

(**) Laboratorio VacSal. Instituto de Biotecnología y Biología Molecular, Departamento de Ciencias Biológicas, Facultad de Ciencias Exactas, Universidad Nacional de La Plata y CCT-La Plata, CONICET. Calles 47 y 115 (1900) La Plata, Argentina.

Abstract

The incidence of the highly contagious respiratory disease named pertussis or whooping cough has been increasing for the past two decades in several countries despite the highly extended vaccination. The reasons for this resurgence are a matter of discussion and, while trying to understand this complex problem, new strategies that include more boosters for adolescents and adults have been adopted in many countries in an attempt to improve the control of the disease. However, the impact of these measures on infants (the risk age group) is not clear. In this context mathematical models are being increasingly used to study the disease transmission and to estimate the impact of different control strategies. In previous work, we developed an age structured deterministic mathematical model with 9 epidemiological classes to evaluate the effect of an adolescent booster on pertussis infant incidence [1]. We have also applied the model to explore different possible causes for pertussis resurgence that are compatible with observed epidemiological data [2]. In this contribution, recent improvements introduced into the model to evaluate the effect of delays in the administration of the first three vaccination doses are described. The

methodology involves the consideration of additional epidemiological classes to keep track of the number of doses administered to the population independently of their immune status [3]. Using data gathered from vaccination centers in urban and suburban areas in an Argentine city, we evaluated the impact on infant incidence of reducing the observed delays in vaccine agoscdministration. We conclude that reducing delays in vaccination or improving the coverage of the first doses are measures with a high potential impact on the risk age group, clearly higher than the inclusion of an adolescent or adult booster at a given age. Robustness of the results was checked for different sets of parameters representing different possible epidemiological scenarios.

Bibliography

[1] "Modeling pertussis transmission to evaluate the effectiveness of an adolescent booster in Argentina". G.Fabricius, P.Bergero, M.Ormazabal, A.Maltz and D. Hozbor. Epidemiology and Infection 141, 718-734 (2013).

[2] "Modelling the effect of changes in vaccine effectiveness and transmission contact rates on pertussis epidemiology". P. Pesco, P.Bergero, G. Fabricius and D. Hozbor. Epidemics 7, 13-21 (2014).
[

3] "Mathematical modeling of delayed pertussis vaccination in infants". P. Pesco, P.Bergero, G. Fabricius and D. Hozbor. Accepted for publication in Vaccine on 1st July 2015.

Granuloma formation in leishmaniasis

Avner Friedman

Department of Mathematics, Ohio State University and Mathematical Biosciences Institute, USA

Abstract

Leishmaniasis is a parasite disease caused by infection with an obligate intracellular protozoa, called Leishmania. Infection occurs when female sand fly bites a human and injects the parasites. There are two forms of the disease: cutaneous leishmaniasis and visceral leismaniasis (VL). VL infects the liver or the spleen, and may be fatal if not treated. The hallmark of VL is the formation of granulomas, small nodules which contain macrophages infected by the parasite, and immune cells that aim to control the infection, primarily T cells.

In this talk I will present a mathematical model of the disease. The model includes various types of immune cells and the cytokines they produce, as well as the parasites. The model is represented by a system of PDEs within the granuloma, the boundary of which is evolving in time, as "free boundary." Cells from the adaptive immune system are migrating into the granuloma with "strength" which is quantified by a parameter beta.

We apply the model to determine the efficacy of a drug, for different values of beta. We propose the concept that the amount of the drug should be correlated to the patient's immune response parameter beta. Future work will consider the correlation between the negative side effects of the drug and the immune strength of the patient.

This work is joint with Nourridine Siewe, Aziz Yakubu, and Abhay Satoskar

Modelling the Ebola epidemic in West Africa

Sebastian Funk

London School of Hygiene and Tropical Medicine, UK

Abstract

The Ebola epidemic in West Africa has overwhelmed health systems and caused an enormous number of disease and death. In this presentation, I will present the efforts in modelling and analysis of the epidemic performed at the Centre for the Mathematical Modelling of Infectious Diseases (CMMID), and how they have evolved over the course of the outbreak.

Determining best strategies for maternally-targeted pertussis vaccination using an individual-based model

Patricia Campbell, Jodie McVernon, Nicholas Geard (presenting author)

Affiliation (all authors): Modelling and Simulation Unit, Centre for Epidemiology and Biostatistics, Melbourne School of Population Health, The University of Melbourne, Australia

Abstract

Pertussis incidence in some highly vaccinated populations, including Australia, has recently risen to levels not seen since vaccination was introduced more than sixty years ago. Improved diagnostics have contributed to this observed rise, however, increased infant deaths in the United States (US) and United Kingdom (UK) in recent epidemics provide evidence of genuine resurgence. Maternally-targeted vaccination strategies, delivered either antenatally or postnatally ('cocooning'), have been implemented in the US, UK and Australia to protect vulnerable infants, who are at greatest risk of severe outcomes. Questions remain regarding the optimal implementation of maternally-targeted strategies, including the relative benefit of antenatal vaccination over postnatal vaccination and the optimal application for protection over multiple pregnancies.

We simulated pertussis transmission and maternally-targeted vaccination strategies within an individual based model framework. Our model characterises individuals by their sex, age and family composition and is parameterised to represent the Australian population across the 20th century. Four alternative vaccination schedules were simulated: the current National Immunisation Program (NIP) schedule alone; and with postnatal vaccination, antenatal vaccination or antenatal vaccination plus reintroduction of an 18 month booster. We compared infant disease in maternally vaccinating and non-maternally vaccinating households to separately estimate the effectiveness of antenatal and postnatal vaccination strategies across a number of implementation scenarios.

For first-born infants, cocooning resulted in a very small reduction in infections over a ten year period, compared to the NIP alone. Antenatal strategies were more effective than cocooning, as infants also acquired direct protection through passive antibody transfer from their mothers. For subsequent children, with around twice the infection risk of first children, the antenatal strategy combined with reintroduction of an 18 month booster resulted in fewer infections caused by both mothers and older siblings. Vaccinating in every pregnancy was more effective in reducing the risk of infection in subsequent children than in the first pregnancy only. Although an 18 month booster did not provide additional protection for under two month old infants, the benefits of this dose were clearly apparent in the latter stages of the first year of life.

Our results inform optimal implementation approaches for infant protection and provide inputs for cost-effectiveness analyses.

Practical aspects of backward bifurcation in a mathematical model for tuberculosis

David J. Gerberry

Department of Mathematics

Xavier University,

3800 Victory Parkway, Cincinnati, Ohio, 45207, USA

Abstract

In this talk, we examine practical aspects of backward bifurcation for a data-based model of tuberculosis that incorporates features commonly linked to backward bifurcation and new considerations such as the treatment of latent TB infection (LTBI) and the BCG vaccine's interference with detecting LTBI. Understanding the interplay between these multiple factors and backward bifurcation is particularly timely given that new diagnostic tests for LTBI detection could dramatically increase rates of both LTBI detection and vaccination in the coming decades.

Via our analytic thresholds for backward bifurcation, we identify those aspects of TB's complicated pathology that make backward bifurcation more or less likely to occur. We also examine the magnitude of the backward bifurcation produced by the model and its sensitivity to various model parameters. We find that backward bifurcation is unlikely to occur. While increased vaccine coverage and/or increased detection and treatment of LTBI can push the threshold for backward bifurcation into the region of biological plausibility, the resulting bifurcations may still be too small to have any noticeable epidemiological impact.

Bibliography:

[1]. Castillo-Chavez, C., & Song, B. (2004). Dynamical models of tuberculosis and their applications. Mathematical Biosciences and Engineering : MBE, 1(2), 361–404.

[2]. Feng, Z., Castillo-Chavez, C., & Capurro, A. F. (2000). A model for tuberculosis with exogenous reinfection. Theoretical Population Biology, 57(3), 235–247. doi:10.1006/tpbi.2000.1451

[3]. Kribs-Zaleta, C. M., & Velasco-Hernández, J. X. (2000). A simple vaccination model with multiple endemic states. Mathematical Biosciences, 164(2), 183–201.

Density-Dependent Contact Rate: Mobility and Contagion in the London Underground.

Lara Goscè, Anders Johansson.
University of Bristol.

Abstract

The study of how epidemics spread across populations is always a current issue, diseases like influenza, tuberculosis or chickenpox, just to name a few, can seriously affect people well beings and eventually lead to severe complications and death. State of the art mathematical models describing the spread of infectious diseases have, in the last decade, mostly been based on a network theory approach. While this has greatly improved prevoius results by considering heteogeneous descriptions, the relative simplicity of compartmental models has been lost and a real understanding of the link between contacts and new infections is still missing.
In our work we have applied a pedestrian mobility approach to typical epidemiological compartmental studies and obtained a new kind of interdisciplinary research that we believe can highly improve state-of-the-art disease spreading models and control measures. Starting by analysing a microscopical case where people are moving in a corridor we build a density-dependend contact rate and show how it relaxes the well mixed assumption and leads to a whole new range of solution obtained by a priori approach. We then show how highly crowded and confined spaces, such as the stations of the London Underground, constitute highly important and generally neglected hearts of new contagions. Using data obtained from TfL (Transport for London) we implement an accurate transportation model of people travelling by the London Underground with an origin-destination method and by analysing the time spent by passenger in each station at different times of the day we infer the average density.
Results of this work show the times and stations that play a greater role in the spreading mechanism and how better statistical predictions, higher awareness and control, both from single individuals, and authorities, could

help contain the diffusion of infections and also save the government substantial economic losses.

Bibliography

Goscè, L., Barton D. & Johansson, A. Analytical Modelling of the Spread of Disease in Confined and Crowded Spaces. Sc. Rep. 4, 856, (2014).

The ecology of microbes: natural history of Infections

Donato Greco

International Prevention Research Institute

Lyon (France)

Abstract

Microbes have been traditionally seen as our enemies : humans were naturally concerned with the diseases caused by microbes, only recently a wider vision of microbes ecology is taking place : in fact germs are living on our planet from some billions year more than humans and do contribute to many living process including essential human body functions. Only a small fraction of germs are “humanized”: contacts between those and human beings follow several roles on which a growing knowledge have been accumulated. A global vision of the micro world could facilitate the understanding of natural history of infections then helping establishing a positive natural equilibrium between humans and those little friends.

Emerging and re-emerging infections: spillover and eliminations

Donato Greco

International Prevention Research Institute

Lyon (France)

&

ASSET EU Project

Abstract

Life is running at high speed in the germs world : microbial species experience a rapid evolution so to become able to adapt to new hosts but also di disappear and reappear. Modern molecular diagnostic techniques allow for rapid recognition of “new” germs and “new” diseases : most of them resulted from genomic adaptation to new hosts and environments , but also as result of new diagnostic tools.

The spill over of germ species from their original natural environment to new areas is one of the main mechanism to occupy new ecological niches.

Mathematical Assessment of the Role of Climate Change on Malaria Dynamics

Abba Gumel

School of Mathematical and Statistical Sciences

Arizona State University, Tempe, Arizona, USA

Abstract

The talk is based on the design of models for gaining insight into the effect of climate change (loosely measured in terms of temperature variability and rainfall) on the ecology (of malaria vector) and epidemiology of malaria, the deadliest vector-borne disease in humans. Theoretical and simulation results will be discussed.

Contact tracing of tuberculosis in low-burden settings

Giorgio Guzzetta(a,b), Marco Ajelli(b), Denise Kirschner(c) and Stefano Merler(b)

a: Trento RISE, Trento, Italy; b: Bruno Kessler Foundation, Trento, Italy;

c: University of Michigan Medical School, Ann Arbor, USA

Abstract

Tuberculosis (TB) is a potentially fatal disease mediated by the airborne pathogen Mycobacterium Tuberculosis. Active disease is not a common outcome of infection, since in most cases the host immune defences contain the bacterium into a latent state (called latent TB infection or LTBI); however, LTBI can reactivate into disease even several decades after the original infection episodes. In low-burden countries, LTBIs from past epochs of higher prevalence constitute a reservoir for sustained transmission and a main hurdle towards the objective of TB elimination.

A key control measure to keep TB transmission low is contact tracing, consisting in the active screening of close contacts of TB patients, and treatment of both TB and LTBI in those found positive. An assessment of the effectiveness of contact tracing programs through targeted epidemiological studies is difficult and a quantitative evaluation of such programs is still lacking [1-3]. Here, we estimate the impact of contact tracing in Arkansas, USA, as an example of a low-burden setting by using an individual based model of TB transmission dynamics within a realistic, spatially explicit and time-evolving socio-demography. The model is calibrated against TB incidence over time and by age in 2001-2011, and quantitatively validated against multiple independent data sets: a molecular epidemiology study [4], investigating transmission clusters; surveillance data on the proportion of TB in foreign-born individuals [5]; and two large scale studies on infection and disease rates in household [6] and workplace [7] contacts of TB patients. We estimate the effectiveness of different components of contact tracing by comparing the number of TB cases and deaths occurred in Arkansas under the implemented program with model estimates obtained in alternative hypothetical scenarios.

According to our model, the Arkansas contact investigation program avoided about 18.6% [95% CI: 12.1-25.9%] of TB cases and 23.7% [16.4-30.6%] of TB deaths overall between 2001 and 2014; almost half of these were attributable to the investigation of less infectious cases (assessed by sputum smear microscopy). Improving the performance of contact tracing (in terms of the proportion of contacts screened and treated) can contribute significantly to further reducing the burden of TB. Finally, we predict a limited potential for contact tracing towards reducing TB incidence from reactivation in the coming decades.

Bibliography

1) Fox GJ, Dobler CC, Marks GB. Active case finding in contacts of people with tuberculosis. The Cochrane Library. 2011. Issue 9.

2) Begun M, Newall AT, Marks GB, Wood JG. Contact Tracing of Tuberculosis: A Systematic Review of Transmission Modelling Studies. PLoS One. 2013. 8(9): e72470.

3) Fox GJ, Barry SE, Britton WJ, Marks GB. Contact investigation for tuberculosis: a systematic review and meta-analysis. Eur Respir J. 2013. 41: 140–156.

4) Online Tuberculosis Information System (OTIS), National Tuberculosis Surveillance System, United States. U.S. Department of Health and Human Services (US DHHS), Centers for Disease Control and Prevention (CDC), Division of TB Elimination, CDC WONDER Online Database, March 2015.

http://wonder.cdc.gov/tb-v2012.html

5) Berzkalns A, Bates J, Ye W, Mukasa L, France AM, Patil N, et al. The road to tuberculosis (Mycobacterium tuberculosis) elimination in Arkansas; a re-examination of risk groups. PLoS One. 2014. 9(3): e90664.

6) Moran-Mendoza O, Marion SA, Elwood K, Patrick DM, FitzGerald JM. Tuberculin skin test size and risk of tuberculosis development: a large population-based study in contacts. Int J Tuberc Lung Dis. 2007. 11: 1014–1020.

7) Davidow AL, Mangura BT, Wolman MS, Bur S, Reves R, Thompson V, et al. Workplace contact investigation in the United States. Int J Tuberc LungDis. 2003. 7: S446–S452.

When is a structured epidemic model representable by a system of ordinary differential equations?

Mats Gyllenberg

Finnish Centre of Excellence in Analysis and Dynamics Research & Department of Mathematics and Statistics,

University of Helsinki, Finland

Estimating vaccine coverage, quantifying outbreak risk and unravelling different sources of heterogeneity in acquisition of infection using multivariate serological data.

Niel Hens

Interuniversitary Institute for Biostatistics and statistical Bioinformatics, Hasselt University, Belgium

Centre for Health Economics Research & Modeling of Infectious Diseases, Vaccine and Infectious Disease Institute, University of Antwerp, Belgium

Abstract

In the past three decades, vaccine policy has become increasingly informed by the use of cross-sectional serosurvey collections that provide estimates of population immunity. Such studies rely on the assumption that the antibody test correlates well with the level of immunity. Uses of such data include monitoring of the immune status of populations and informing transmission modeling studies, through estimation of the pre-vaccination force of infection and the basic reproduction number in assessments of new vaccine programs. another important use is in model validation, or in improving estimates of model parameters. In recent years, however, there has been considerable development in both the methods used in estimating parameters from sero-survey data and the range of questions that can be asked of such data. Using (series of) cross-sectional serosurvey(s) in which multiple antigens were tested three topics will addressed: estimating vaccine coverage, quantifying outbreak risk in highly vaccinated populations, and unravelling different sources of heterogeneity in acquisition of infection.

Bibliography

Abrams, S., Beutels, P., Hens, N. (2014) Assessing outbreak risk in highly vaccinated populations using spatial seroprevalence data on mumps American Journal of Epidemiology. 179(8), 1006-1017.

Abrams, S., Hens, N. (2015) Modeling individual heterogeneity in the acquisition of recurrent infections: an application to parvovirus B19. Biostatistics 16, 1, 129-

142.

Bollaerts, K., Aerts, M., Faes, C., Shkedy, Z., Van der Stede, Y., P., Beutels, P., Hens, N. (2012) Estimation of population prevalence and force of infection directly from antibody titres. Statistical Modelling. 12, 441-462.

Goeyvaerts, N., Hens, N., Aerts, M. and Beutels, P. (2011) Model structure analysis to estimate basic immunological processes and maternal risk for parvovirus B19. Biostatistics 12, 283-302.

Goeyvaerts, N., Hens, N., Theeten, H., Aerts, M., Van Damme, P., Beutels, P. (2012) Estimating vaccination coverage for the trivalent measles-mumps-rubella vaccine from trivariate serological data. Statistics in Medicine. 31(14), 1432-1449.

Goeyvaerts, N., Leuridan, E., Faes, C., Van Damme, P., Hens, N. Multi-Disease Analysis of Maternal Antibody Decay in Infants Using Non-Linear Mixed Models Accounting for Censoring. Statistics in Medicine. In Press.

Hens, N., Abrams, S., Santermans, E., Theeten, H., Goeyvaerts, N., Lernout, T., Leuridan, E., Van Kerckhove, K., Goossens, H., Van Damme, P., Beutels, P. (2015) Assessing the risk of measles resurgence in a highly vaccinated population: Belgium anno 2013. Euro Surveill. 2015;20(1):pii=20998.

Hens, N., Wienke, A., Aerts, M., Molenberghs, G. (2009) The Correlated and Shared Gamma Frailty Model for Bivariate Current Status Data: An Illustration for Cross-sectional Serological Data. Statistics in Medicine. 28, 2785-2800.

Santermans, E., Goeyvaerts, N., Melegaro, A., Edmunds, J.W., Faes, C., Aerts, M., Beutels, P., Hens, N. (2015) The social contact hypothesis under the assumption of endemic equilibrium: elucidating the transmission potential of VZV in Europe. Epidemics, 11, 14-23.

Wood, J.G., Goeyvaerts, N., MacIntyre, C.R., Menzies, R.I., McIntyre, P.B., Hens, N. (2015) Estimating vaccine coverage from serial trivariate serological data in the presence of waning immunity. Epidemiology. May;26(3):381-9.

Modelling influenza A at the human-animal interface

Edward Hill1, Thomas House2, Michael Tildesley3

1 Centre for Complexity Science and Warwick Infectious Disease Epidemiology Research Centre, University of Warwick, Coventry, UK.

2 School of Mathematics, The University of Manchester, Manchester, UK.

3 School of Veterinary Medicine and Science, University of Nottingham, Leicestershire, UK.

*Corresponding author: Edward Hill, email:Edward.Hill@warwick.ac.uk

Abstract

Type A influenza inhabits many hosts and has many strains [1]. The biology and epidemiology of influenza A is radically different depending on the host species: while ducks are essentially asymptomatic carriers of all type A influenza strains, in other birds and mammals influenza A can be lethal. Very occasionally, humans become infected with a virus derived from non-human sources. These are essentially novel to humans. Due to the viruses meeting with little or no established resistance, they can, following mutation and adaptation to their new host, spread relatively easily in the human species. This can give rise to a localised outbreak that may develop into a worldwide influenza pandemic.

Despite this, there is a worrying gap in the modelling of spillover transmission from animals to humans [2]. While the within-species dynamics of influenza in poultry and humans has been well studied, we present a spatial model incorporating cross-species transmission. The model is focused at a local level, to incorporate locations of farms and markets where livestock and humans are in close contact. This framework is applied to H5N1 epidemics in Bangladesh occurring from 2007 to 2011, which resulted in a limited number of confirmed

human cases in addition to dramatically affecting the poultry production sector. We present preliminary modelling results and analyse the impact of different demographic characteristics upon disease transmission, with possible computational techniques to parameterise the model outlined. This work will provide insights regarding the risk to humans associated with avian influenza outbreaks and preferred control strategies, across both human and livestock species, in the event of future epidemics.

Bibliography

[1] R Jennings and RC Read, Influenza: Human and Avian, Royal Society of Medicine Press 2nd ed. (2006).

[2] JO Lloyd-Smith et al, Epidemic Dynamics at the Human-Animal Interface, Science 326(5958) 1362-1367 (2009).

Quantification of Bird-to-Bird and Bird-to-Human Infections for H7N9 Avian Influenza Outbreak

Ying-Hen Hsieh (1,2*), Jianhong Wu (3,4), Jian Fang (3,4,5), Yong Yang (3), Jie Lou (6)

1. Department of Public Health, China Medical University, Taichung, Taiwan,

2. Center for Infectious DiseaseEducation and Research, China Medical University, Taichung, Taiwan,

3. Department of Mathematics andStatistics, York University, Toronto, Ontario, Canada,

4. Centre for Disease Modelling, York University,Toronto, Ontario, Canada,

5. Department of Mathematics, Harbin Institute of Technology, Harbin, China,
6.Department of Mathematics, Shanghai University, Shanghai, China.

Abstract

Since February 19, 2013 to May1, 2015,?a total of 657 laboratory-confirmed cases of human infection with avian influenza A(H7N9) viruses were identified in China, including at least 261 deaths. We developed a novel, simple and effective compartmental modeling framework for transmissions among (wild and domestic) birds as well as from birds to human, to infer important epidemiological quantifiers, such as basic reproduction number for bird epidemic, bird-to-human infection rate and turning points of the epidemics, for the epidemic via human H7N9case onset data and to acquire useful information regarding the bird-to-human transmission dynamics. Estimated basic reproduction number for infections among birds, obtained by fitting 2013 human case data, is 4.10 and the mean daily number of human infections per infected bird is 3.16 [3.08, 3.23]. The turning point of 2013 H7N9 epidemic is pinpointed at April 16 for bird infections and at April 9 for bird-to-human transmissions. Our result reveals very low level of bird-to-human infections, thus indicating minimal risk of widespread bird-to-human infections of H7N9 virus during the outbreak. Moreover, the turning point of the human epidemic, pinpointed at shortly after the implementation of full-scale control and intervention measures initiated in early April, further highlights the impact of

timely actions on ending the outbreak. This is the first study where both the bird and human components of an avian influenza epidemic can be quantified using only the human case data.

Multi-scale modelling of foot-and-mouth disease

B. Hu - University of Warwick and The Pirbright Institute
M. J. Tildesley - University of Nottingham
L. Danon - University of Bristol
J. L. Gonzales - Central Veterinary Institute
S. Gubbins - The Pirbright Institute

Abstract

Foot-and-mouth disease (FMD) is a highly contagious viral infection that affects cloven-hoofed animals. It is of major socio-economic importance, with past epidemics causing devastating impacts on previously disease-free countries. Understanding how the virus spreads is vital for the development of successful control strategies.

Current models use the farm, rather than the animal, as the fundamental epidemiological unit. This assumes that the infection within a farm is fast, with all animals being simultaneously infected. We address this assumption using a two-scale model which integrates the spread of the disease between animals within a farm and between-farm transmission.

The between-farm model follows existing work in classifying individual farms as being either susceptible, infectious or removed. Transmission then depends on three factors; the susceptibility of the target farm, transmissibility of the source farm and the distance between them. A transmission kernel is used to describe the relative risk of transmission as a function of distance. Unlike in existing models in which the transmissibility depends solely on the number of animals on the farm, we assume it is proportional to the number of infectious animals on the farm. This is determined by simulating spread between animals on each infected farm. These dynamics are described using a susceptible-exposed-infected-recovered (SEIR) model for multiple species (cattle, pigs and sheep).

The model is implemented in a Bayesian framework to allow us to integrate data from a range of sources and to facilitate inclusion of parameter uncertainty in model predictions. In particular, priors for the within-farm parameters are

derived using data from transmission experiments. Subsequent parameter estimation was carried out by fitting the model to the 2001 UK outbreak. We compare our results to those of the existing models to quantify the impact of the within-farm dynamics and the relationship between the within- and between-farm models.

Modeling Ebola Virus Dynamics: Implications for Therapy

Shingo Iwami, Department of Biology, Kyushu University, Japan & PRESTO, JST, Japan

Abstract *

EBOV RNA levels in the blood increases rapidly, and after reaching a peak (or plateau level), the RNA copies declines until it falls below the detection limit (6,200 RNA copies/ml of serum).

The RNA levels in the blood in patients who died are on average 100-fold higher than those in patients who survived. And, 108 RNA copies/ml is considered as an approximate threshold which predicts a fatal outcome with a positive predictive capability of 90%.

Here we quantitatively analyze the mean EBOV RNA copies/ml of serum from 18 survivors (non-fatal case) and 27 nonsurvivors (fatal case) after the onset of symptoms, and revealed EBOV dynamics. Furthermore, based on our mathematical model and estimated parameter values, we would like to investigate how delay of treatment initiation, or how incomplete blocking of virus replication affect the clinical outcomes of EBOV patients depending on the mechanism of action for antiviral drugs or vaccines.

Bibliography

[1] Quantification of viral infection dynamics in animal experiments. Iwami S, Koizumi Y, Ikeda H, Kakizoe Y. Front Microbiol. 2013 Sep 10;4:264.
[2] Rapid diagnosis of Ebola hemorrhagic fever by reverse transcription-PCR in an outbreak setting and assessment of patient viral load as a predictor of outcome. Towner JS1, Rollin PE, Bausch DG, Sanchez A, Crary SM, Vincent M, Lee WF, Spiropoulou CF, Ksiazek TG, Lukwiya M, Kaducu F, Downing R, Nichol ST. J Virol. 2004 Apr;78(8):4330-41.

Modelling the impact of treatment on transmission dynamics of HIV and hepatitis C

Mirjam Kretzschmar

Centre for Infectious Disease Control, RIVM, & University Medical Centre Utrecht, The Netherlands

Abstract

"Treatment as prevention" has been designated by WHO as the most important strategy for reducing the burden of HIV worldwide. It is expected that scaling up HIV treatment to higher levels of coverage will have substantial impact on HIV incidence or can even lead to elimination in populations with generalized epidemics. More recently, similar hopes have arisen for elimination of hepatitis C virus following the development of new treatment options for this bloodborne infection. We used deterministic models to describe HIV disease progression, variable infectivity, and the impact of treatment on transmission. We studied the elimination threshold and investigated under what conditions of treatment uptake and dropout elimination of HIV is feasible. We derived explicit expressions for the basic reproduction number and the elimination threshold. Using estimates of exponential growth rates of HIV during the initial phase of epidemics we investigated for which populations elimination is within reach. The infectivity during the primary stage of infection plays an important role in determining the possible impact of treatment on HIV incidence. Empirical estimates of the epidemic growth rate from phylogenetic studies were used to assess the potential for elimination in specific populations. For hepatitis C, we investigated how reinfection after cure may affect possible elimination prospects in populations of injecting drug users. Here, a model for HIV and HCV coinfection was used. To monitor the impact of treatment on HIV transmission, population viral load metrics such as the community viral load have been introduced. Using our deterministic model, we investigated under which circumstances population viral load metrics that can be measured among the population in care give a good picture of the force of infection that susceptible individuals are exposed to.

Numerical algorithm of constructing the individual-based mathematical model of the epidemiology of Tuberculosis

S.I. Kabanikhin 1, 2 , O.I. Krivorotko 1, 2 , A.A. Romanyukha 3, 4 , A.A. Borisov 5 , S.E. Belilovsky 5 , V.N. Kashtanova 1 and A.S. Karkach 3

1 Novosibirsk State University, Novosibirsk, Russia
2 Institute of Computational Mathematics and Mathematical Geophysics of SB RAS, Novosibirsk, Russia
3 Institute for Numerical Mathematics, Russian Academy of Science, Moscow, Russia
4 Lomonosov Moscow State University, Moscow, Russia
5 Moscow Scientific and Clinical Center for Tuberculosis Control, Moscow Health Department, Moscow, Russia
Email: krivorotko.olya@mail.ru

Abstract

The epidemic of tuberculosis (TB) is accompanied by quantitative as well as qualitative changes of this disease specific to different regions [1-3]. It is necessary to develop an action plan to identify and treat patients for the prediction of the epidemic spread in a particular region. The mathematical modeling namely the development of individual mathematical model describing the process of the propagation of infection in the population is one of the most effective methods for prediction of the epidemic spread. Such models are described by a system of nonlinear ordinary differential equations (ODE). The coefficients of these systems characterize the features of population and disease spread. The average parameters such as speed of the disease expansion, parameter of transmissibility, the likelihood of infection expansion, parameter of the mortality, etc. are known for any region. We plan to refine the parameters of infection and population using above data and the statistical information about infected individuals, overlooked patients with bacillary and non-bacillary TB , etc. at previous years. The algorithm consists in the numerical regularization of inverse and ill-posed problems for ODE systems [4], iterative and statistical methods. Developed algorithm will give the degree of deviation

of infection and population parameters from the average after processing the results of the statistics for the previous few years. Thus, the World Health Organization will be able to predict the infectious disease epidemic comparing simulation results with historical data. The problem of parameters fitting in the mathematical model of the Tuberculosis spread in Moscow using the statistical information on the number of infectious and non-infectious individuals over the preceding 5 years is numerically investigated [3].

Bibliography

1. K.K. Avilov and A.A. Romanyukha. Mathematical modeling of tuberculosis propagation and patient detection // automation and remote control. – 2007. – Vol. 68, No. 9. – P. 1604-1617.
2. E.A. Nosova and A.A. Romanyukha. Mathematical model of HIV-infection transmission and dynamics in the size of risk groups // Mathematical Models and Computer Simulations. – 2013. – Vol. 25, No. 1. – P. 45-64.
3. K.K. Avilov, A.A. Romanyukha, S.E. Borisov, E.M. Belilovsky, O.B. Nechaeva and A.S. Karkach. An approach to estimating tuberculosis incidence and case detection rate from routine notification data // The International Journal of Tuberculosis and Lung Disease. – 2015. – Vol. 19, No. 3. – P. 288-294.
4. S.I. Kabanikhin. Inverse and Ill-Posed Problems: Theory and Applications. Berlin: de Gruyter, 2011.

Characterizing the transmission potential of zoonotic infections

Adam J Kucharski & W John Edmunds, Centre for the Mathematical Modelling of Infectious Diseases, London School of Hygiene & Tropical Medicine

Abstract

The transmission potential of a novel infection depends on both the inherent transmissibility of a pathogen, and the level of susceptibility in the host population. However, distinguishing between these pathogen- and population-specific properties typically requires detailed serological studies, which are rarely available in the early stages of an outbreak.

Deriving a multiple-type branching process model that incorporates age-stratified social mixing patterns, we present a method for characterizing the transmission potential of subcritical infections, which have effective reproduction number $R<1$, from readily available data on the size of outbreaks. We show that the approach can identify the extent to which outbreaks are driven by inherent pathogen transmissibility and pre-existing population immunity, and can generate unbiased estimates of the effective reproduction number. We also discuss how such models can be used to assess the transmission potential of infections such as avian influenza, monkeypox and MERS-CoV.

Novel estimation of mosquito longevity using a Bayesian meta-analysis.

Ben Lambert (Zoology, Oxford University), Ace North (Zoology, Oxford University), Charles Godfray (Zoology, Oxford University).

Abstract:
Anopheles mosquitoes are the only vector for the disease *malaria*, but remarkably little is known about them. In this paper I will present a meta-analysis of a recently-compiled database (1), which we have used to arrive at coherent estimates of Anopheline longevity. It is increasingly important to know Anopheles bionomic parameters in order to calibrate existent epidemiological models to be able to estimate the impact of interventions *a priori *(see for example (2), and (3), (4) for more recent examples). The primary method for estimating Anopheles characteristics is mark-release-recapture experiments (MRR). These field studies are costly, and often only result in a moderate amount of data from which to base estimates. In this paper, we used a hierarchical Bayesian model applied to a newly published database of over 100 separate MRR time series, in order to produce cohesive estimates of mosquito longevity. This methodology allows us to address a number of pertinent questions: which mathematical models of MRR experiments produce better estimates of mortality? Do Anopheles senesce? And are there differences in mosquito longevity that vary by species?

Bibliography

(1) Guerra et al. *A global assembly of adult female mosquito mark-release-recapture data to inform the control of mosquito-borne pathogens*. Parasites & Vectors 2014, 7:276.

(2) Smith & McKenzie. *Statics and dynamics of malaria infection in Anopheles mosquitoes.* Malaria Journal 3.1 2004:13.

(3) Eckhoff et al. *From puddles to planet: modeling approaches to vector-borne diseases at varying resolution and scale.* Current Opinion in Insect Science 2015, 10:118-123.

(4) North et al. *Modelling the spatial spread of a homing endonuclease gene in a mosquito population.* Journal of applied ecology 2013, 50, 1216-1225.

Challenges in Application of Optimal Control to Spread of Infectious Diseases

Urszula Ledzewicz

Southern Illinois University Edwardsville, USA

e-mail: uledzew@siue.edu

joint work with Heinz Schaettler

Washington University, St. Louis, MO, USA

Abstract

In the field of epidemiology a lot of attention has been given to analysis of mathematical models with the tools of dynamical systems from the point of view of equilibria, their stability, regions of attraction and particularly the role of the quantity called basic reproduction number denoted as R_0. The value of this quantity allows to determine whether the disease will spread or eventually die out. However, relatively less attention is given to the matter of controlling the spread of disease through external activities like vaccination of the susceptible population or treatment of infected. There are other aspects like quarantine of exposed population or sanitation efforts that are expensive and are best treated as optimal control problems. In these formulations the proper choice of objective is important. Its role will be illustrated on an analysis of a simple SIR model with the objective takes into account the minimization of the infected population along with the weighted cost of these treatments, so called L1 objective. This approach will be compared with the L2 formulation of the objective (linear versus quadratic in the control). The interpretation of both will be discussed as well as the mathematical aspects of optimality, i.e. the verification of the sufficient conditions.

A modeling approach to predict the flu epidemic using the prevalence data

Sergey V. Ivanov, ITMO University, Saint Petersburg, Russia
Vasiliy N. Leonenko, ITMO University, Saint Petersburg, Russia

Abstract:

Influenza is a widespread infectious disease with a strong economic impact. In this study we use methods of mathematical epidemiology to distinguish the epidemic outbreak from the seasonal increase in morbidity and to evaluate the predictability of epidemic based on the observed prevalence. For the sake of disease dynamics simulation a state-space influenza model is proposed which takes into the account the demographic, mobility, and vaccination data. The methods under study are verified on the historical data of flu incidence in big Russian cities over the last thirty years.

Bibliography

[1] S. Hanson and P. Hanson, “The travel-activity patterns of urban residents: dimensions and relationships to sociodemographic characteristics,” Econ. Geogr., pp. 332–347, 1981.
[2] J. L. Bowman and M. E. Ben-Akiva, “Activity-based disaggregate travel demand model system with activity schedules,” Transp. Res. Part A Policy Pract., vol. 35, no. 1, pp. 1–28, 2001.
[3] C. J. Ketcham and G. E. Stelmach, “Movement control in the older adult,” Technol. Adapt. aging, pp. 64–92, 2004.
[4] H. W. Hethcote, “The mathematics of infectious diseases,” SIAM Rev., vol. 42, no. 4, pp. 599–653, 2000.
[5] M. Kermark and A. G. Mckendrick, “Contributions to the mathematical theory of epidemics. Part I,” in Proc. R. Soc. A, 1927, vol. 115, no. 5, pp. 700–721.
[6] http://www.who.int/mediacentre/factsheets/fs211/en/
[7] Mills C.E., Robins J.M., Lipsitch M. Transmissibility of 1918 pandemic

influenza. Nature, 2004. Vol. 432. No. 7019. P. 904–906.
[8] Casagrandi R., Bolzoni L., Levin S.A., Andreasen V. The SIRC model and influenza A. Mathematical Biosciences, 2006. No. 200. P. 152–169.

STIs on dynamic sexual networks

KaYin Leung (a) (b), Mirjam Kretzschmar (b) (c), Odo Diekmann (a)

(a) Mathematical Institute, Utrecht University, The Netherlands
(b) Julius Center for Primary Care and Health Sciences, University Medical Center Utrecht, The Netherlands
(c) National Institute for Public Health and the Environment, The Netherlands

Abstract

What is the influence of concurrent partnerships on the spread of sexually transmitted infections? Our aim is to develop tools for gaining insight in this question (which has generated considerable debate in the context of HIV in sub-Saharan Africa). To this end we model the spread of a sexually transmitted infection on a dynamic partnership network. Individuals in the network may have a varying number of simultaneous partnerships with a maximum number of partners at a time. The network is dynamic; partnerships are formed and dissolved over time and individuals enter and leave the population due to demographic turnover. Transmission can occur in partnerships between infectious and susceptible individuals. Based on our model analysis we find that concurrent partnerships could drive an HIV epidemic. In this talk we discuss results and open problems related to the network structure, infectious disease dynamics and the concurrency question.

Global and individual oriented descriptors in stochastic epidemic models

MJ Lopez-Herrero,
Faculty of Statistical Studies,
Complutense University of Madrid, Spain

Abstract:
In this talk new indicators for disease spread in stochastic epidemic models are introduced. These include global system oriented descriptors and individual oriented ones. We study both continuous and discrete descriptors on stochastic compartmental models. To illustrate how results can be used to investigate properties of the infection spread we include an application to outbreaks of head lice in UK schools.

Bibliography:

(1) Artalejo JR and Lopez-Herrero MJ (2014) Stochastic epidemic midels: New behavioral indicators of the disease spreading. Applied Mathematical Modelling 38, 4371 - 4387
(2) Stone P, Wilkinson-Herbots H and Isham V (2008) A stochastic model for head lice infections. Journal of Mathematical Biology 56, 743-763

Herpes Zoster

Piero Manfredi

Pisa University, Italy

Joint work with: Guzzetta G, Poletti P, Del Fava E, Scalia Tomba G, Merler S.

Abstract

Herpes zoster (HZ) is caused by the reactivation of the varicella zoster virus (VZV) as cell mediated immunity (CMI) goes down (e.g. with ageing). Hope-Simpson formulated (1965) the “exogenous boosting” hypothesis (EBH), according to which further infective exposures to VZV may boost CMI, resulting in a protective effect against HZ. Inclusion of the exogenous boosting hypothesis in VZV transmission models predicts a large transient wave in natural HZ incidence following mass varicella immunization. The fear of this HZ “boom” is a main responsible of the current stall of varicella vaccination in Europe. In this talk, I summarize recent results from a model incorporating a further noteworthy Hope-Simpson’s hypothesis, stating that each VZV re-exposure increases CMI protection against HZ to levels higher than those conferred by previous ones. The “progressive immunity” model fits well available European HZ data, suggesting that the mechanism may be critical in shaping HZ patterns. The model suggests counter-intuitive implications of varicella immunization in relation to vaccine-related HZ and the epidemiology of HZ after varicella elimination. I conclude by discussing the challenges for future VZV research.

The role of climatic factors in shaping mosquito population dynamics: the case of Culex pipiens in Northwestern Italy

Giovanni Marini, Trento University, Trento (Italy)

Piero Poletti, Bocconi University, Milan (Italy)

Stefano Merler, Fondazione Bruno Kessler, Trento (Italy)

Andrea Pugliese, Trento University, Trento (Italy)

Roberto Rosà, Fondazione Edmund Mach, San Michele all'Adige (Italy)

Abstract

Culex pipiens mosquito is a species widely spread across Europe and represents a competent vector for many human diseases such as West Nile virus (WNV) [1], which has been circulating in many European countries during last years, causing hundreds of human cases [2]. Rigorous surveillance of mosquito density and control programs based on the reduction of the mosquito population represent key components of disease containment and prevention [3, 4]. Therefore, in order to design appropriate control strategies it is crucial to investigate the influence of climatic factors on the dynamics of vector populations during a typical breeding season.

To understand which are the main determinants of the high heterogeneity observed in Piedmont region (Northwestern Italy) in *Culex pipiens* abundance across different seasons, we developed a density dependent mathematical model that takes explicitly into account the mechanisms of diapause characterizing the overwintering of adult mosquitoes (driven by the daylight duration) [5], and the role played by temperature, which strongly affects both developmental and death rates of different life

stages of *Culex pipiens* [6, 7]. The model was calibrated by performing a Bayesian statistical analysis of weekly capture data gathered in our study site from 2000 to 2011.

Our analysis suggests that the high heterogeneity characterizing the dynamics of mosquito density among different years is driven by differences in the temporal patterns of temperature and in the larval carrying capacity associated to different breeding seasons. Specifically, high temperatures during early spring may anticipate the onset of the breeding season, while higher temperatures during late spring are associated with longer seasons. On the opposite, high temperatures during the summer can reduce the *Culex pipiens* abundance by increasing the adult mortality during this period. Our results show that higher density of adult mosquitoes are associated to higher larval carrying capacities which result positively correlated with spring precipitations suggesting that more rain during spring can create more breeding sites.

Finally, our simulations show that the initial number of adults does not affect the vector abundance of a specific season, suggesting that two consecutive years might be unrelated and that the inter-seasonal heterogeneity might not be influenced by the adults' ability of overwintering.

Bibliography

1. Zeller HG, Schuffenecker I. "West Nile Virus: an overview of its spread in Europe and the Mediterranean Basin in contrast to its spread in the Americas." *European Journal of Clinical Microbiology & Infectious Diseases* 23, no. 3 (March 2004): 147–156.

2. European Centre for Disease Prevention and Control. "Annual epidemiological report 2014 – emerging and vector-borne diseases." Stockholm: ECDC; 2014.

3. Colborn JM, Smith KA, Townsend J, Damian D, Nasci RS, Mutebi JP. "West Nile Virus Outbreak in Phoenix, Arizona-2010: Entomological Observations

and Epidemiological Correlations." *Journal of the American Mosquito Control Association* 29, no. 2 (June 2013): 123–32.

4. Kilpatrick AM, Pape J. "Predicting Human West Nile Virus Infections with Mosquito Surveillance Data." *American Journal of Epidemiology* 178, no. 5 (September 2013): 829–35.

5. Spielman A, Wong J. "Environmental Control of Ovarian Diapause in Culex Pipiens." *Annals of the Entomological Society of America* 66, no. 4 (July 1973): 905–7.

6. Loetti V, Schweigmann N, Burroni N. "Development Rates, Larval Survivorship and Wing Length of Culex Pipiens (Diptera: Culicidae) at Constant Temperatures." *Journal of Natural History* 45, no. 35–36 (September 2011): 2203–13.

7. Ciota AT, Matacchiero AC, Kilpatrick AM, Kramer LD. "The Effect of Temperature on Life History Traits of Culex Mosquitoes." *Journal of Medical Entomology* 51, no. 1 (January 2014): 55–62.

Dynamics of Low and High Pathogenic Avian Influenza in Wild and Domestic Bird Populations

N. Tuncer(b), Juan Torres(a), M. Martcheva(a), M. Barfield(c), R.D. Holt(c)

a) Department of Mathematics

University of Florida

Gainesville, FL 32611

maia@ufl.edu

b) Department of Mathematical Sciences

Florida Atlantic University

Boca Raton,FL 33431

ntuncer@fau.edu

c) Department of Biology

University of Florida

Gainesville, FL 32611

Key words: Avian influenza, H5N1, reproduction numbers

Abstract

Avian influenza H5N1 is at present the most dangerous zoonotic disease infecting wild and domestic birds. Should the virus mutate and become efficiently human-to-human transmittable, a pandemic will occur with high mortality. Avian influenza H5N1 exists in two forms: Low pathogenic (LPAI) and high pathogenic (HPAI). In this talk we build a model of LPAI and HPAI in wild and domestic birds. Birds, wild and domestic, who have been priorly infected with LPAI are partially protected against HPAI. We compute the relevant reproduction numbers andinvasion reproduction numbers. We find that the systems has a disease-free equilibrium, LPAIonly equilibrium, HPAI-only equilibrium and at least one coexistence equilibrium. Furthermore,the LPAI-only equilibrium and HPAI-only equilibrium are locally asymptotically stable under appropriate conditions on the reproduction numbers. In contrast, the coexistence equilibrium can lose stability and oscillations are possible. We show

that the oscillations are caused by the cross-immunity and can exist in the wild bird system, separate from the domestic bird system.

For a pathogen circulating in a multi-species system, species A is called a sink (source), if the pathogen cannot (can) sustain itself in species A without the inflow of infectives from other species. We investigate the sink/source status of LPAI and HPAI in wild and domestic birds.

The impact of changing demography on the epidemiology of varicella and herpes zoster

Valentina Marziano (1,2), Piero Poletti (1,3), Giorgio Guzzetta (1,4), Marco Ajelli (1), Piero Manfredi (5) and Stefano Merler (1)

1. Center for Information Technology, Bruno Kessler Foundation, Trento, Italy
2. Department of Mathematics, University of Trento, Trento, Italy
3. DONDENA Centre for Research on Social Dynamics, Bocconi University, Milan, Italy
4. Trento Rise, Trento, Italy
5. Department of Economics and Management, Pisa University, Pisa, Italy

Abstract:

The first contact with Varicella Zoster Virus (VZV) causes varicella disease. After recovery, the virus persists in a latent form and may reactivate later in life triggering Herpes Zoster (HZ) [1]. Studies suggest that the individual risk of VZV reactivation is reduced by re-exposures to varicella-infected individuals, called boosting events, whose frequency critically depends on the level of VZV circulation in the population [2,3]. The aim of this work is to investigate the role of demographic changes in the epidemiology of VZV-related diseases. We focus on the case of Spain since in this country, as well as in other industrialized countries, an increase of HZ incidence has been observed even prior to the introduction of varicella vaccination [4,5]. To this purpose, we developed a stochastic, individual-based model for varicella and HZ informed with historical demographic data.
Results obtained show that the strong decline of the birth rate during the last century has led to a decrease in the circulation of VZV, to a reduction in the frequency of boosting events and, as a consequence, to a growing incidence of HZ. Moreover, this growth is predicted to continue in the coming decades under different scenarios of demographic projections. Our results suggest that demographic changes are at least partly responsible for the observed variations in the epidemiology of HZ. Their

consideration is thus essential for estimating the outcomes and the cost-effectiveness of varicella and HZ immunization programmes.

Bibliography:

[1] Donahue JG, Choo PW, Manson JE, Platt R. 1995 The incidence of herpes zoster. Arch. Intern. Med. 155, 1605 –1609. (doi:10.1001/archinte.1995. 00430150071008)

[2] Terada K, Kawano S, Yoshihiro K, Morita T. 1993 Proliferative response to varicella-zoster virus is inverse related to development of high levels of varicella-zoster virus specific IgG antibodies. Scand. J. Infect. Dis. 25, 775 –778. (doi:10.3109/00365549309008578)

[3] Ogunjimi B, Smits E, Hens N, Hens A, Lenders K, Ieven M, Van Tendeloo V, Van Damme P, Beutels P. 2011 Exploring the impact of exposure to primary varicella in children on varicella-zoster virus immunity of parents. Viral Immunol. 24, 151 –157. (doi:10.1089/vim.2010.0031)

[4] Perez-Farinos N, Ordobas M, Garcıa-Fernandez C, Garcıa-Comas L, Canellas S, Rodero I, Gutierrez-Rodrıguez A, Garcıa-Gutierrez J, Ramırez R. 2007 Varicella and herpes zoster in Madrid, based on the sentinel general practitioner network: 1997– 2004. BMC Inf

[5] Reynolds MA, Chavez SS, Harpaz R, Lopez AS, Seward JF. 2008 The impact of varicella vaccination program on herpes zoster epidemiology in the United States: a review. J. Infect. Dis. 197, S224– S227. (doi:10.1086/522162)

Investigating Social Contact Structures and Time Use Patterns in the Manicaland Province of Zimbabwe

Alessia Melegaro

DONDENA Centre for Research on Social Dynamics and Public Policy & Department of Policy Analysis and Public Management, Bocconi University, Milan, Italy

Abstract

The demographic transition (i.e., declining fertility and mortality, increasing urbanization) that is charecterising Sub Saharan African (SSA) countries is clearly affecting population social structures, such as households, schools and workplace enviornments. As a consequence of these changes, individual daily routines and social mixing patterns, which are both key determinants of infectious disease transmission, are also expected to evolve over time, potentially affecting, in the long term, the outcomes of public health interventions. Diary-based data on social contact patterns and time use were collected in two sites, one rural and one urban, from Manicaland, Zimbabwe to quantify mixing patterns and daily routines relevant to infection transmission, to assess within country differences, and to investigate the key determinants of the numbers of contacts in key socio-demographic settings (home, school, work, and the general community).

In total 1139 diaries were collected and included detailed information on background socio-demographic characteristics, contact and time use data. Overall, the estimated number of daily contacts was found to be 10.8, with a significant difference between urban and rural sites (11.6 vs. 10.2). Students and workers resulted as the most socially active groups with respectively an average number of contacts of 13.5 and 12.8.

In comparison with previous EU studies, the ensuing contact matrix showed a lower age assortativeness, detectable almost exclusively among school-aged children, and relatively higher intergenarational contacts (i.e.; parents/relatives with children). These differences are possibly the consequence of the younger

age distribution, the higher proportion of extended families and the different use of time (67.3% of overall daytime spent at home and only 2.5% at work). Finally, whereas differences in the number of work-related contacts can be ascribed to differences in the time at work, variations in the number of contacts at school are explained by school attendance and class-size. The current work represent the first attempt to gather and combine social contacts and time use data with the aim of better understanding the key determinants of infection transmission within populations still characterised by extremly high burden of diseases and childhood mortality . These data are critical to evaluating realistically the effects of public health interventions such as vaccination strategies in low income settings. Moreover, the generated social contact matrices in a urban and a rural setting of SSA will contribute to strengthening our knowledge on the evolution of mixing patterns in changing demographic environments.

Understanding EVD in West Africa: epidemiological investigation and computational modeling

Stefano Merler
Fondazione Bruno Kessler, Trento (Italy)

Abstract

The 2014 epidemic of Ebola virus disease in West Africa defines an unprecedented health threat. In July 2014 an outbreak of EVD started in Pujehun district (Sierra Leone) and on January 10th 2015 the district was the first to be declared Ebola-free by local authorities. Here we combine epidemiological investigation and modeling techniques to reconstruct the main characteristics of the outbreak and to evaluate the impact of the implemented intervention measures. Specifically, i) we reconstructed the transmission chain in the district (obtaining information on the main routes of infection transmission and on the distribution of the basic reproduction number); ii) we estimated the key time period of the epidemic (e.g. incubation period, serial interval); iii) we estimated the impact of all intervention measures (e.g. the probability of hospitalization of Ebola cases, the probability of unsafe burials, the percentage of cases detected and isolated through contact investigation); iv) we calibrated a detailed model of EVD transmission informed with all the above information to estimate the impact of all considered interventions in the Pujehun district. This allowed us to clarify the reasons behind the successful local containment of the outbreak and to give quantitative insights into the best options for containing an emerging Ebola epidemic at the source.

Differing social encounter profiles by local government area of residence in greater Melbourne, Australia

Jodie McVernon [1], David A Rolls [2], Nicholas L Geard [1], Deborah J Warr [3], Paula M Nathan [1], Garry L Robins [2], Philippa E Pattison [2], James M McCaw [1, 4]

1 Modelling and Simulation Unit, Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Australia

2 Melbourne School of Psychological Sciences, The University of Melbourne, Australia

3 McCaughey VicHealth Community Wellbeing Unit, Melbourne School of Population and Global Health, The University of Melbourne

4 School of Mathematics and Statistics, The University of Melbourne, Australia

Abstract

Background: Models of infectious disease increasingly seek to incorporate heterogeneity of social interactions to more accurately characterise disease spread. We measured attributes of social encounters in two areas of Greater Melbourne, using a telephone survey.

Methods: A market research company conducted computer assisted telephone interviews (CATIs) of residents of the Boroondara and Hume local government areas (LGAs), which differ markedly in ethnic composition, age distribution and household socioeconomic status. Survey items included household demographic and socio-economic characteristics. Respondents reported locations visited during the preceding day, including social encounters involving two-way conversation or physical contact.

Results: The overall response rate was 37.6%, higher in Boroondara [n=650, (46%)] than Hume [n= 657 (32%)] residents. Survey complexity made conduct through the CATI format challenging, with implications for representativeness and data quality. Marked heterogeneity of encounter profiles was observed across age groups and locations. Household settings afforded greatest opportunity for prolonged close contact with others, particularly between women and children of pre- and primary-school age. Young and middle-aged men, on the other hand, reported more age-assortative mixing, often with non-household members. Preliminary comparisons between LGAs suggested that

mixing occurred in different settings. In addition, gender differences in mixing with household and non-household members, including strangers, were observed by area.

Conclusions: Survey administration by CATI was challenging, but rich data were obtained, revealing marked heterogeneity of social behaviour. Marked dissimilarities in patterns of prolonged close mixing were demonstrated by gender. In addition, preliminary observations of between-area differences in socialisation warrant further evaluation.

Control Strategies for TB Epidemics

Fabio Augusto Milner

School of Mathematical and Statistical Sciences

Arizona State University

Abstract

A model for tuberculosis incorporating migration of susceptible and infected individuals into the population is presented and analyzed. Infected individuals are structured by time since infection to include a long and variable latency period, and individuals with active TB have an increased mortality rate. A control problem is formulated and analyzed, minimizing the impact of infection by controlling immigration and/or treating infected individuals before they develop active TB.

Optimal Resource Allocation for Infectious Diseases Prevention Programs

Semu Mitiku (PhD), Department of Mathematics, Addis Ababa University, P.O.Box 80333, Addis Ababa, Ethiopia

Abstract

Developing countries get the major part of the fund for their disease prevention programs from global funding organizations. The allocation of such funds usually pass through several levels of decision making bodies who have their own specific parameters to control and specific objectives to achieve. However, these decisions are made mostly in a heuristic manner and may lead to non-optimal allocation of the scarce resources. In this work we will address the issue of optimal way of allocating resources for disease prevention and control programs in developing countries where the allocation passes through several levels.

Combining existing epidemiological models with the kind of interventions being on practice, we propose a 3-level hierarchical decision making model in optimally allocating such resources. The optimality will be checked in terms of the effectiveness of the interventions carried out and the actual impact of the intervention both at international and community levels.

Bibliography

1. M. L. Brandeau, G. S. Zaric, A. Richter, Resource allocation for control of infectious diseases in multiple independent populations: beyond cost-effectiveness analysis, Journal of Health Economics (2003) 22, 575 – 598.

2. G. S. Zaric, M. L. Brandeau, A little Planning Goes a Long Way: Multilevel Allocation of HIV Prevention Resources, Medical Decision Making (2007) 27, 71 - 81.

3. N. Graves, K. Halton, W. Jarvis, Economics and Preventing Healthcare Acquired Infection, Springer Science+Business Media, LLC (2009).

4. A. T. Woldemariam, S.M. Kassa, Systematic Evolutionary Algorithm for a general Multilevel Stackelberg Problems with bounded decision variables (SEAMSP), Ann. Oper. Res. (2015) 229: 771-790.

5. A. M. Kassa, S.M. Kassa, A Branch-and-Bound Multi-parametric Programming Approach for General Non-convex Multilevel Optimization with Polyhedral Constraints, to appear on Journal of Global Optimization (Springer) (2015).

Estimating the protective effect of case isolation: A case study of smallpox

Hiroshi Nishiura, The University of Tokyo, Japan

Abstract

There has been an enourmous progress in the study design and theory that allow us to estimate the protective effect of vaccination both at individual and population levels. On the contrary, the effectiveness of case isolation has never been explicitly estimated, and it is technically not feasible to randomly assign infected individuals to isolation. Here I propose an epidemiological modeling method to infer the effectiveness expressed as the relative reduction in the frequency of secondary transmissions in the presence of isolation measure. Using the renewal equation model, two pieces of information are extracted, i.e., the time interval between successive cases and the distribution of the number of secondary cases produced by a single primary case. For the exposition, we analyze the infection tree of a smallpox epidemic in 1950s that involves not only the time of illness onset and time of isolation for each case but also the network that shows who acquired infection from whom. It is shown that the serial interval and generation time are shortened by effective isolation, and moreover, the average number of secondary cases per single primary case is also reduced. The proposed method allows us to estimate the effectiveness from retrospectively collected contact tracing data.

Bibliography

Nishiura H, Yan P, Sleeman CK, Mode CJ. Estimating the transmission potential of supercritical processes based on the final size distribution of minor outbreaks. J Theor Biol. 2012;294:48-55.

Nishiura H, Eichner M. Infectiousness of smallpox relative to disease age: estimates based on transmission network and incubation period. Epidemiol Infect. 2007;135(7):1145-50.

Nishiura H, Schwehm M, Kakehashi M, Eichner M. Transmission potential of primary pneumonic plague: time inhomogeneous evaluation based on historical

documents of the transmission network. J Epidemiol Community Health. 2006;60(7):640-5.

Optimal Control for the NIV Virus

Filipa N. Nogueira and Maria do Rosario de Pinho

Abstract

NiV virus was initially isolated and identified in 1999 during an outbreak of encephalitis and respiratory illness in Malaysia and Singapore. In 2001, NiV was again identified as the causative agent in an outbreak of human disease occurring in Bangladesh. Since 2001 many outbreaks have been reported in Asia. Outbreaks occur almost annually in Bangladesh with a dead rate of almost 100%. It is known that infected bats' droppings, urine and saliva contaminate date palms in Bangladesh. The drink of raw sap or fruits is much appreciated in Bangladesh. These can be contaminated and so humans become infected when they drink it. Once a individual gets infected the disease easily spreads by horizontal transmission: through sneezing, coughing and body fluids. There is no cure or vaccine to such virus.

Here we propose an optimal control approach to the control of such disease via education campaigns and isolation of infected individual. Our starting point is the paper [1], where real data is used.

Bibliography

[1] OPTIMAL CONTROL OF NIPAH VIRUS (NIV) INFECTIONS: A BANGLADESH SCENARIO, MHA Biswas, Journal of Pure and Applied Mathematics: Advances and Applications Volume 12, Number 1, 2014, Pages 77-104

Epidemic Outbreaks In Networks With Equitable Or Almost-Equitable Partitions

Stefano Bonaccorsi∗, Stefania Ottaviano ∗†, Delio Mugnolo‡, Francesco De Pellegrini †

∗Mathematics Department, University Of Trento,Via Sommarive 14, 38123 Povo (Trento), Italy
†Create-Net, Via Alla Cascata 56/D, 38123 Povo (Trento), Italy
‡Lehrgebiet Analysis, Fakultat Fur Mathematik Und Informatik, Fern Universitat In Hagen, 58084
Hagen, Germany

Abstract

We study the diffusion of epidemics on networks, describing the epidemic process as a continuous-time Markovian individual-based SIS model. We use a first-order mean-field approximation (NIMFA) of the exact model, appeared recently in literature [1,2,3], to represent the time-dependent infection probability of each individual in the network.

First we provide a complete analysis of the global dynamics, in the homogeneous case, that allows us to identify the epidemic threshold. This kind of rigorous analysis was missing for NIMFA in literature. The same type of analysis can be extended effortless in the case of heterogeneity setting [4].

Our main objective is understanding how the spatial structure of a population determines the systems' dynamics. To this respect, a network structure describes the proximity relation of individuals. In turn, proximity determines individual's interactions which can spread the contagion within the population. In this context, we explore a specific spatial regime: we consider a model for the diffusion of epidemics in a population that is partitioned into local communities (clouds, households,...). The model we are interested in may well represent the diffusion of computer viruses or epidemics among families or schools. For such a reason, we neglect the effect of migration between communities as in some recent works [5,6].

The gross structure of hierarchical networks of this kind can be described by a quotient graph. The rationale of this approach is that the epidemic process within communities is faster compared to the rate at which it spreads across communities [7].

One of the main results is that the spectral radius of this much smaller quotient graph (which only captures the macroscopic structure of the community network) is all we need to know in order to decide whether the overall healthy-state defines a globally asymptotically stable or an unstable equilibrium. Indeed the spectral radius is related to the epidemic threshold of the system. Moreover we prove that above the threshold exists another steady-state that can be computed using a lower-dimensional dynamical system associated with the evolution of the process on the quotient graph. Our investigations are based on the graph-theoretical notion of equitable partition and of its recent and rather flexible generalization, that of almost equitable partition.

Bibliography

[1] P. Van Mieghem, J. Omic and R. E. Kooij, Virus Spread in Networks, IEEE/ACM Transaction on Networking, 17:1–14, 2009.

[2] P.Van Mieghem, and R. van de Bovenkamp, Accuracy criterion for the mean-field approximation in SIS epidemics on networks, Physical Review E, 91(3): 032812, 2015.

[3] E. Cator and P. Van Mieghem, Nodal infection in Markovian SIS and SIR epidemics on networks are non-negatively correlated, Physical Review E, 89(5): 052802, 2014.

[4] A. Lajmanovich and J. A. Yorke , A deterministic model for gonorrhea in a nonhomogeneous population, Mathematical Biosciences 28.3, 221-236, 1976

[5] V. Colizza, A. Vespignani: Epidemic modeling in metapopulation systems with

heterogeneous coupling pattern: theory and simulations. Journal of theoretical biology 251.3, (2008) 450-467

[6] C. Poletto, S. Meloni, V. Colizza, Y. Moreno, and A. Vespignani: Host mobility drives pathogen competition in spatially structured populations. PLoS computational biology 9.8 , (2013): e1003169

[7] S. Bonaccorsi, S. Ottaviano, F. De Pellegrini, A. Socievole and P. Van Mieghem, Epidemic outbreaks in two-scale community networks, Physical Review E, 90(1): 012810, 2014.

A simple model of HIV epidemic in Italy: the role of the anti-retroviral treatment.

F. Papa(1), F. Binda(2), G. Felici(1), M. Franzetti(2), A. Gandolfi(1), C. Sinisgalli(1), C. Balotta(2)

(1) Istituto di Analisi dei Sistemi ed Informatica 'A. Ruberti' - CNR, Roma, Italy
(2) Dipartimento di Scienze Biomediche e Cliniche 'L. Sacco', Sezione di Malattie Infettive e Immunopatologia, Università degli Studi di Milano, Milano, Italy

Abstract

A simple model is proposed to describe the HIV epidemic in Italy for the years 2003-2023. To represent the intra-host disease progression, the infected (not treated) population is distributed over four compartments in cascade according to the CD4 counts. The last compartment represents individuals in the AIDS state. A further compartment is added to account for infected people under ART (anti-retroviral therapy). As a first simplifying assumption we take as susceptible the general population. Data from the Italian Operative AIDS Center (COA) of the National Institute of Health (ISS) [1], from the National Institute for Statistics (ISTAT) and from ARCA database, concerning the years 2003-2013, have been used to calibrate the model. A satisfactory agreement with the data has been obtained. Predictions for the years 2014-2023 are then done evidencing the role of ART, in particular evaluating the influence of early treatments on the epidemic evolution. The model is intended as an initial step towards a more complex model for the evolution of anti-retroviral drug resistance, in which, following the approach outlined in [2], susceptible individuals can be infected by different virus strains resistant to different drug classes, and mutations can occur during treatment.

Bibliography

[1] Camoni L, Regine V, Stanecki K, et al. Estimates of the number of people living with HIV in Italy. Biomed Res Int 2014 (2014).
[2] Smith RJ, Okano JT, Kahn JS, Bodine EN, Blower S.: Evolutionary

dynamics of complex networks of HIV drug-resistant strains: the case of San Francisco. Science 327, 697-701 (2010).

Application of Large Deviations to Epidemiological models

Etienne Pardoux, Brice Samegni Kepnou
I2M, Aix–Marseille University

Abstract :
The goal of this talk is to present the application of Large Deviations, and more specifically of the Freidlin–Wentzell theory [1] to epidemiological models. We start from a stochatic compartmental epidemiological model driven by Poisson processes, whose solution Z(t) takes values in Rd, d being the number of compartments (for instance 3 in the case of a SIR model), and describes the proportions of the population of total size N (which for instance can be assumed fixed)
in the various compartments. The equation is driven by mutually independent standard Poisson processes, and involves the rates Nβj(z), where this is the rate at which the proportions of the population in the various compartments jump from z to z + hj/N, 1 ≤ j ≤ k.

It is well known that if the βj's are bounded and locally Lipschitz continuous, then as N → ∞, Z(t) converges a.s. locally uniformly in t towards the solution X(t) of the ODE with coefficient b(x)=\sum_{j=1}^k \beta_j(x) h_j. The stochastic equation for Z(t) is then a small random perturbation of the ODE. In order to apply here the Freidlin–Wentzell theory, we need to develop a theory of Large Deviations for Poisson driven SDEs, where the rates are allowed to vanish as they do at the boundary of the set {z ∈ Rd, zi ≥ 0,\sum_i zi ≤ 1}. This is the content of [3], which develops the generalization necessary for epidemiological models of the results in [7].

With those results in hand, we can precise the time it takes for the process Z(t) to make a large deviation from the solution X(t) of the ODE, e.g. to leave the basin of attraction of a local equilibrium of the ODE.

The application which we have in mind, and which we intend to describe in this talk, is to evaluate the time it takes for an endemic situation to cease. We intend to illustrate our results on specific examples of variants of the classical SIS model, like the SIV model [4] and the SIS model with two levels of susceptibility [6].

Bibliography

[1] M.I. Freidlin and A.D. Wentzell, Random perturbations of dynamical systems, Springer Verlag 1984.

[2] P. Kratz, E. Pardoux and B. Samegni Kepnou, Numerical methods in the context of compartmental models in epidemiology, ESAIM : Proceedings and Surveys 48, 169–189, 2015.

[3] P. Kratz and E. Pardoux, Large deviations for epidemiological models, to be submitted.

[4] C. M. Kribs–Zaleta and J.X. Velasco–Hernandez, A simple vaccination model with multiple endemic states, Mathematical Biosciences 164, 183–201, 2000.

[5] T. Kurtz, Strong approximation theorems for density dependent Markov chains, Stochastic Processes and their Applications 6 223–240, 1978.

[6] M. Safan, H. Heesterbeek and K. Dietz, The minimum effort required to eradicate infections in models with backward bifiurcation, J. Math. Biol. 53, 703–718, 2006.

[7] A. Shwartz and A. Weiss, Large deviations with diminishig rates, Mathematics of Operations Research 30 281–310, 2005.

Density dependent diffusion and spread of epidemics in a metapopulation model

A. Avinyó, M. Pellicer, J. Ripoll, J. Saldaña
Departament d'Informàtica, Matemàtica Aplicada i Estadística
Universitat de Girona, Campus Montilivi, 17071 Girona, Spain

Abstract:

In this work we explain the results of the recent paper [2], in which we extend the previous works [1] and [3] to a model where the impact of a density-dependent diffusion on the spread of the epidemics is considered. This is, to our knowledge, the main novelty of the present work.

More concretely, we are dealing with a mean-field type model as a system of ordinary differential equations which combines (random, memoryless) the movement of individuals among patches (nodes) with a local SIS-epidemics within each patch and a density-dependent number of contacts. The main difference now is a diffusion coefficient that depends in a non-linear way on the density of individuals of the departing patch. Actually, two types of such a dependence are considered: namely, the positive and negative ones. They allow us to model two types of observed migration phenomena: emigration from heavily populated locations (due to competition, for instance) or from low-density areas (due to aggregation or conspecific attraction, for instance), respectively.

We determine the equilibrium driven by the migration process without epidemics and quantify the percentage of heavily/lightly populated areas corresponding to each migratory diffusion pattern. Our analytical approach reveals that the optimal migratory diffusion for controlling the epidemic spreading consists in strengthen the emigration from populous areas to sparse ones. Moreover, depending on the migration pattern, epidemic outbreaks not always occur in more populated patches as one may expect, but it may happen only in mid-size ones or even only in the lowest populated ones.

Bibliography

[1] D. Juher, J. Ripoll, and J. Saldaña. Analysis and Monte Carlo simulations of a model for the spread of infectious diseases in heterogeneous metapopulations, Physical Review E 80, 041920 (2009).

[2] J. Ripoll, A. Avinyó, M. Pellicer, J. Saldaña. Impact of nonlinear migration floows on epidemic outbreaks in heterogeneous metapopulations. Submitted (2015)

[3] J. Saldaña. Continuous-time formulation of reaction-diffusion processes on heterogeneous metapopulations, Physical Review E 78, 012902 (2008).

A multi-strain multi-scale approach to HIV evolutionary epidemiology

Lorenzo Pellis

arwick Mathematics Institute, University of Warwick, Coventry, CV4 7AL, United Kingdom

Joint work with: KA Lythgo and C Fraser

Abstract

The long infectious period and the high mutation rate characteristic of human immunodeficiency virus (HIV) offer ample opportunity for within-host evolution to change the composition of pathogen genotypes within a host during the course of an infection. This alters the availability of genotypes at the time of transmission and hence affects the pathogen genotype distribution at the population level. Therefore, in order to understand the evolution of HIV at the epidemiological level, a multi-scale modelling approach is needed.

I will present a model that can simultaneously include an explicit description of the within-host evolutionary dynamics of a large number of competing strains, their impact on between-host transmission events and the resulting epidemic dynamics.

I will conclude that the topology of the within-host adaptive landscape strongly affects how virulence evolves at the epidemiological level. If viral reproduction rates increase significantly during the course of infection, the viral population will evolve a high level of virulence even though this will reduce the probability for the virus to transmit between hosts (short-sighted evolution). However, if reproduction rates increase more modestly, as data suggest, our model predicts that HIV virulence will be only marginally higher than the level that optimises between-host transmission (long-sighted evolution).

This work provides a clear mathematical tool to investigate the contrasting evolutionary pressures a pathogen might be subjected to when comparing evolution at the within- versus between-host scale, and identifies or suggests possible reasons that can explain the currently observed HIV virulence patterns.

Time permitting, I will also show how multi-scale models can also explain the extraordinary variation in HIV viral load (several orders of magnitude) among untreated individuals.

Agent-based models and ill-posed problems

Perminov V. D., BioTeckFarm LtD., Moscow, Russian Federation

Abstract

It is well known that evaluation of parameters for any mathematical model is always a difficult problem. This is especially true for agents-based models (ABMs) because an evaluation of agent's parameters can be made only based on available information from a higher level of a complex system. Because of information at a higher level is an aggregation of data at the agents level such problems can be ill-posed ones. It means a problem under consideration can have a non-unique or unique but unstable solution. In the latter case numerical solution of the problem has to be based on very special algorithms.
In this talk I am going to overview problems that arise for ABMs with different numbers of emergent patterns. In particular I am going to tell about new approach to creation of the ABM for an influenza epidemic spreading in cities. The proposed ABM can be used for past epidemics to estimate the efficiency or inefficiency of undertaken interventions, to propose new ones and to reveal its advantages, shortcomings and cost. This ABM is the first one that under some conditions can be used to model the possible dynamics of coming epidemics or pandemics.

Evaluating vaccination strategies for reducing infant respiratory syncytial virus infection in low-income settings

Piero Poletti (a,b), Stefano Merler (b), Marco Ajelli (b), Piero Manfredi (c), Patrick K. Munywoki (d), David J. Nokes (d,e), Alessia Melegaro (a)

a) Dondena Centre for Research on Social Dynamics and Public Policy, Department of Policy Analysis and Public Management, Universitá Commerciale L. Bocconi, Milan, Italy; b) Center for Information Technology, Bruno Kessler Foundation, Trento, Italy; c) Department of Economics and Management, Pisa University, Pisa, Italy; d) Kenyan Medical Research Institute (KEMRI), Kilifi, Kenya; e) School of Life Sciences and WIDER, University of Warwick, Warwick, UK;

Abstract:

Respiratory syncytial virus (RSV) is a leading cause of lower respiratory tract disease and related hospitalization of young children in least developed countries [1,2]. Individuals are repeatedly infected, but it is the first exposure, often in early infancy, that results in the vast majority of severe RSV disease [3,4]. Unfortunately, due to immunological immaturity, infants are problematic RSV vaccine targets. Several trials are ongoing to identify a suitable candidate vaccine and target group, but no immunization program is yet in place [5,6]. In this work, an individual-based model that explicitly accounts for the socio-demographic population structure is developed to investigate RSV transmission patterns in a rural setting of Kenya and to evaluate the potential effectiveness of alternative population targets in reducing RSV infant infection. We find that household transmission is responsible for 39% of infant infections and that school-age children are the main source of infection within the household, causing around 55% of cases. Moreover, assuming a vaccine-induced protection equivalent to that of natural infection, our results show that annual vaccination of students is the only alternative

strategy to routine immunization of infants able to trigger a relevant and persistent reduction of infant infection (on average, of 35.6% versus 41.5% in 10 years of vaccination). Interestingly, if vaccination of pregnant women boosts maternal antibody protection in infants by an additional 4 months, RSV infant infection will be reduced by 31.5%. These preliminary evaluations support the efforts to develop vaccines and related strategies that go beyond targeting vaccines to those at highest risk of severe disease.

Bibliography

1. Nair H, Nokes DJ, Gessner BD, Dherani M, Madhi SA, Singleton RJ, *et al*.: Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. ***Lancet*** 2010, 375:1545-55.

2. Nokes DJ, Ngama M, Bett A, Abwao J, Munywoki PK, English M, *et al*.: Incidence and severity of respiratory syncytial virus pneumonia in rural Kenyan children identified through hospital surveillance. *Clin Infect Dis.* 2009, 49:1341-9.

3. Ohuma EO, Okiro EA, Ochola R, Sande CJ, Cane PA, Medley GF, *et al*.: The natural history of respiratory syncytial virus in a birth cohort: the influence of age and previous infection on reinfection and disease.* Am J Epidemiol.* 2012, 176:794-802.

4. Berkley JA, Munywoki P, Ngama M, Kazungu S, Abwao J, Bett A, *et al*.: Viral etiology of severe pneumonia among Kenyan infants and children. *J Am Med Assoc.* 2010, 303:2051-7.

Polack FP, Karron RA: The future of respiratory syncytial virus vaccine development. *Pediatr Infect Dis J.* 2004, 23:65-73.

5. Anderson LJ, Dormitzer PR, Nokes DJ, Rappuoli R, Roca A, Graham BS:

Strategic priorities for respiratory syncytial virus (RSV) vaccine development. ***Vaccine*** 2013, 31:209-15.

6. Polack FP, Karron RA: The future of respiratory syncytial virus vaccine development. *Pediatr Infect Dis J.* 2004, 23:65-73.

Epidemic models with multiple strains and partial cross-immunity

Andrea Pugliese

Mathematics Department, Trento University, Italy

Abstract

For many infectious diseases there exist different strains, with some degree of cross-immunity among them. Recognizing this factor may be relevant both for understanding infection dynamics, and for public health policy.

Here I analyse two model:

- in the first I consider two pathogen strains with complete cross-immunity, and study the potential effects of a vaccine with differential efficacy againts the two;

- the second is a simplified model for flu, with two strains with partial cross-immunity, aspecific temporary immunity and waning of specific immunity. I show, mainly through simulations, the effects of these factors on the infection dynamics.

Lessons from past influenza pandemics: signature features from the third pandemics

Caterina Rizzo

National Institute of Health, Rome, Italy

Inferring pertussis epidemiology

Pejman Rohani

University of Michigan, USA

Abstract

In this talk I will focus on pertussis, a bacterial respiratory infection whose incidence has increased in a number of countries that have achieved high vaccine coverage. In many countries, the finger of suspicion has been pointed towards modern acellular vaccines and consequently booster doses have been introduced into the routine immunization schedule. To identify effective pertussis booster schedules, in terms of the frequency, age and coverage, we used an age-stratified transmission model within a genetic algorithm setting. We found that effective strategies were sensitive to the assumed underlying cause of vaccine failure, including low coverage, primary or secondary failure or bacterial evolution. This work emphasized the need to pinpoint the precise immunological traits of pertussis vaccines. To achieve this, we then used likelihood-based inference to fit a family of transmission models to incidence reports from different regions of Italy, with the aim of establishing the mode of vaccine failure and its overall impact on pertussis epidemiology. While we were unable to uniquely identify the mechanism behind vaccine failure, we were able to demonstrate that the acellular pertussis vaccine has achieved high impact in Italy, with a substantial reduction in transmission.

Impact of heterogeneity in sexual behavior on possible elimination of HIV transmission with test-and-treat strategy

Ganna Rozhnova 1, Maarten F. Schim van der Loeff 3,4, and Mirjam E. Kretzschmar 1,2

1 Julius Center for Health Sciences and Primary Care, University Medical Centre Utrecht, 3584CX, Utrecht, The Netherlands
2 Centre for Infectious Disease Control, National Institute of Public Health and the Environment, 3721MA, Bilthoven, The Netherlands
3 Department of Infectious Disease Control, Public Health Service Amsterdam, 1018WT, Amsterdam, The Netherlands
4 Center of Infection and Immunity Amsterdam, Academic Medical Center, 1105AZ, Amsterdam, The Netherlands

Abstract

Recently, a large trial conducted in 34 countries provided evidence that starting antiretroviral therapy as soon as possible is advantageous for health prospects of HIV infected persons. It is expected that new treatment guidelines will recommend implementation of a test-and-treat strategy globally [1]. While much work has been devoted to investigation of conditions under which a test-and-treat strategy would eventually lead to elimination of HIV from a population [2,3], behavioral determinants of HIV transmission dynamics and how heterogeneity in sexual behavior influences the impact of treatment on HIV transmission have received less attention. Using a deterministic model, we present a framework which allows a systematic investigation into the effects of various mixing patterns in a population of men who have sex with men, stratified by rates of partner change, on the basic reproduction number, treatment effects and prospects of elimination. We find that both the level of overdispersion in the distribution of the number of sexual partners and mixing between population subgroups have a large influence on the elimination threshold and endemic prevalence of HIV. Higher assortativeness of mixing and more heterogeneity in risk behavior lead to higher elimination threshold as quantified by the effective reproduction number. As assortativeness of mixing increases, the distribution of HIV infection across risk groups becomes more skewed with high prevalence in small high risk subgroups. Increasing the level of screening and treatment uptake decreases the effective reproduction number. The

specific value of treatment coverage at which it becomes smaller than 1, and thus elimination is feasible, depends on the type of mixing pattern. In particular, we conclude that it is not feasible to eliminate HIV from populations with high levels of assortative mixing by activity level without additional intervention strategies, even if treatment uptake is as high as 90% annually. Finally, we discuss how to use the developed framework as a way of extracting information on behavioral heterogeneity from existing data, particularly assortativeness of mixing, which are otherwise hard to measure in population surveys.

Bibliography

[1] National Institutes of Health. Starting antiretroviral treatment early improves outcomes for HIV-infected individuals.http://www.nih.gov/news/health/may2015/niaid-27.htm May 27, 2015.

[2] R. M. Granich, C. F. Gilks, C. Dye, K. M. De Cock, and B. G. Williams. Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. Lancet, 373:48-57, 2009.

[3] M. E. Kretzschmar, M. F. Schim van der Loeff, P. J. Birrell, D. De Angelis, and R. A. Coutinho. Prospects of elimination of HIV with test-andtreat strategy. Proceedings of the National Academy of Sciences USA, 110:1553815543, 2013.

How to analyze epidemic data in the emerging phase

Gianpaolo Scalia-Tomba

Department of Mathematics, University Rome “Tor Vergata”, Rome, Italy

Abstract

The increasing interest in initial phase inference on disease outbreaks has generated a corresponding interest in the concept of generation time as a descriptor of the "time scale" of the disease. The standard definition of generation time is simple, viz. the average time between the infection of a secondary case and that of the primary. However, a closer study reveals many interesting complications, in particular regarding how to observe and do statistics on generation times. These complications and possible remedies will be presented and discussed.

Chaos and noise in population biology

Nico Stollenwerk

Lisbon University, Portugal

Computational epidemiology does more than forecast

Alessandro Vespignani

Department of Physics, Northeastern University, USA

Abstract

Recent years have witnessed the development of data driven models of infectious diseases rooted in the combination of large–scale data mining techniques, computational approaches and mathematical modeling.

Although these models are increasingly used to support public-health decisions they are often under debate by only considering their value as forecasting tools.

Here I will discuss, by using specific modelling examples of the H1N1 pandemic and the West Africa Ebola epidemic, how computational models can be used in real time to provide situational awareness, intervention planning and projections, and the identification of factors that fundamentally influence the course of an outbreak.

Coinfection by opportunistic diseases: a time scales approach.

Ezio Venturino

Dipartimento di Matematica ``Giuseppe Peano'',

Universita' di Torino, Italy.

Email: ezio.venturino@unito.it

Abstract

We present an approach for the investigation of opportunistic diseases, i.e. those ailments that better affect a population when in it already another epidemic spreads, the primary disease.

The main reason is due to the already damaged or weakened immune system of the individuals caused by the first epidemic, or to the resistance developed to antibiotics.

When two infections coexist in an individual, there are two possibilities.

A superinfection phenomenon arises if the second invasion is possibly performed by a different strain of the established disease.

Superinfection by different strains of HIV results in coinfection with tuberculosis. Another example is AIDS involving coinfection of end-stage HIV with opportunistic parasites and polymicrobial infections like the vector-borne Lyme disease.

Coinfection occurs instead when individuals are simultaneously infected by two independent pathogens irrespective of whether they arise at the same time or one of them favors the secondary invasion. Examples are for instance bacterial superinfection in a viral respiratory disease or infection of a chronic hepatitis B carrier with hepatitis D virus.

The primary disease in general weakens over a long period the individual immune system, allowing the sudden appearance of the opportunistic disease.

This feature suggests the use of time scales separation in the model, distinguishing respectively in it a slow and a fast process.

Approximate aggregation techniques can then be applied to get a reduced, lower dimensional system showing the same asymptotic information of the complete model.

Our findings indicate that the outcome of the primary infection is deeply affected by the secondary disease.

An outbreak of the opportunistic disease may allow the primary disease to persist, but for some parameter values ranges the opportunistic disease may drive infected individuals to extinction.

Under certain conditions, the model behavior is more sensitive to the opportunistic disease recovery rate than to the transmission rate, suggesting a way to fight coinfection problems.

Bibliography

P. Auger, R. Bravo de la Parra, J.C. Poggiale, E. S\'anchez, T. Nguyen Huu, Aggregation of variables and applications to population dynamics. In: P. Magal, S. Ruan (Eds.), Structured Population Models in Biology and Epidemiology, Lecture Notes in Mathematics, vol. 1936, Mathematical Biosciences Subseries. Springer, Berlin, 2008, p. 209--263

P. Auger, J.-C. Poggiale, E. S\'anchez, A review on spatial aggregation methods involving several time scales, Ecological Complexity 10, 12--25

S.D. Lawn (2004). AIDS in Africa: the impact of coinfections on the pathogenesis of HIV-1 infection. Journal of Infection 48 (1): 1--12

Marcos Marv\'a, Ezio Venturino, Rafael Bravo de la Parra, A time scales approach to coinfection by opportunistic diseases, Journal of Applied Mathematics, vol. 2015, Article ID 275485, 10 pages, 2015. doi:10.1155/2015/275485.

P.D. Mitchell, K.D. Reed, J.M Hofkes (1996). Immunoserologic evidence of coinfection with Borrelia burgdorferi, Babesia microti, and human granulocytic Ehrlichia species in residents of Wisconsin and Minnesota. Journal of clinical microbiology 34 (3): 724--7

M. Singer and S. Clair (2003). Syndemics and Public Health: Reconceptualizing Disease in Bio-Social Context. Medical Anthropology Quarterly, New Series, Vol. 17, No. 4 pp. 423--441

J. Smith (2011). Superinfection drives virulence evolution in experimental populations of bacteria and plasmids. Evolution, 65, 3, 831—841

Heterogeneous Population Dynamics and Scaling Laws near Epidemic Outbreaks

A.Widder (1), C. Kuehn (2)
(1) ORCOS, Institute of Mathematical Methods in Economics, Vienna, University of Technology
(2) Institute for Analysis and Scienti?c Computing, Vienna, University of Technology

Abstract

In this paper, we focus on the influence of heterogeneity and stochasticity of the population on the dynamical structure of a basic susceptible-infected-susceptible (SIS) model. First we prove that, upon a suitable mathematical reformulation of the basic reproduction number, the homogeneous system and the heterogeneous system exhibit a completely analogous global behaviour. Then we consider noise terms to incorporate the fluctuation effects and the random import of the disease into the population and analyse the influence of heterogeneity on warning signs for critical transitions (or tipping points). This theory shows that one may be able to anticipate whether a bifurcation point is close before it happens. We use numerical simulations of a stochastic fast-slow heterogeneous population SIS model and show various aspects of heterogeneity have crucial influences on the scaling laws that are used as early-warning signs for the homogeneous system. Thus, although the basic structural qualitative dynamical properties are the same for both systems, the quantitative features for epidemic prediction are expected to change and care has to be taken to interpret potential warning signs for disease outbreaks correctly.

Intervening in Heterogenous Epidemics: Insights from the Renewal Equation, and Application to Acute HIV Transmission

Chris Wymant
Department of Infectious Disease Epidemiology, Imperial College London, UK

Joint work with Francois Blanquart, Christophe Fraser, and the BEEHIVE Collaboration

Abstract

The severity of HIV infection varies considerably between individuals. Set?point viral load (SPVL) - a predictor of clinical outcomes such as time to progression to AIDS - varies over several orders of magnitude. While estimates of the extent of SPVL heritability vary widely (6% to 59%), the fact that it is heritable shows that it is in part controlled by the virus itself. We investigate how, and how much, using viral whole-genome data and clinical follow up for around 700 patients from the Netherlands and the UK, sampled between 1985 and 2014. The patients were identified as recently infected; the samples were taken less than two years after the first positive test and before antiretroviral therapy. I will present a novel pipeline for high-throughput, accurate reconstruction of whole viral genomes from the raw genetic data. Phylogenies derived from these data provide a more precise dating of the origin of HIV in Europe, and give a picture of viral mixing. By fitting evolutionary models to the phlyogenetic and phenotypic data we estimate that the heritability of SPVL increased from 17% in 1990 to 34% in 2010, due to increasing genetic variance. This means that extreme values of SPVL become more frequent over time, with potential implications for transmission and disease progression. The special case of multiply-infected individuals and its clinical relevance will also be discussed.

LIST OF POSTERS

SURNAME	NAME	AFFILIATION	POSTER TITLE
Bishop	Alex	University of Warwick	Household models of soil-transmitted helminthias
Bonacini Elena	Soresina Cinzia	Dipartimento di Matematica e Informatica, Università degli Studi di Parma	Time-optimal control strategies in SIR epidemic m
clamer	valentina	Dip matematica Trento	MCMC Methods applied to epidemic outbreaks
Giardina	federica	Department of Mathematics, Stockholm University	HIV epidemic in Sweden: can we infer the structu contact networks from pathogen phylogenies?
Kyncl	Ian	National Institute of Public Health, Srobarova 48 100 42 Praha 10, Czech Republic	Effects of temperature extremes on cardiovascula mortality/morbidity and influenza attributable mo Czech Republic
Moua	Yi	ESPACE-DEV, UMR 228, Université de Guyane, Cayenne, French Guiana	Sampling bias corrections in Maxent: evaluation o
Ong	Karen	New York University School of Medicine	Hybrid Continuous-time / Discrete-time Markov M Bacterial Transmission and Colonization in Hospita
pellis lorenzo	lorenzo	Warwick Mathematics Institute, University of Warwick, Coventry, CV4 7AL, United Kingdom	A multi-strain multi-scale approach to HIV evoluti epidemiology
pio ferreira	claudia	Departamento de Bioestatística, Instituto de Biociências de Botucatu, Unesp - Câmpus de Botucatu, Distrito de Rubião Júnior, S/N CEP: 18618-970 - Botucatu / SP, Brasil	Interactions between dengue serotypes in a huma network

SMID	JOOST	Institute for Risk Assessment Sciences, Utrecht University	Framework model for source attribution of extend beta-lactamase/AmpC beta-lactamase producing
Voronov	Dimitri	Novosibirsk State University and Institute of Computational Mathematics and Mathematical Geophysics of SB RAS, Novosibirsk, Russia	Numerical solution of inverse problem of Tubercu Moscow. Identifiability concepts
Wester	Tom	Department of Mathematics, United States Naval Academy, Annapolis MD, USA	Analysis and Simulation of a Mathematical Model Virus Dynamics in vivo