CCS'15 Satellite Meeting
Contagion '15 – 4th edition

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BOOK OF ABSTRACTS*

Pejman Rohani (University of Georgia, US)
Using complex systems approaches to understand and control infectious diseases
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.

Joel Miller (Monash University, Australia)
Epidemics of dose-dependent infections
Many infections have different outcomes depending on the initial dose an individual receives. In general a larger dose makes people more likely to get sick, but also likely to be sicker and thus more infectious. We use the spread of cholera in a metapopulation model to demonstrate possible dynamics. We dichotomize the population into symptomatic and asymptomatic infections. The asymptomatic individuals contribute a small amount of cholera to the water supply while symptomatic individuals contribute much more. Ingestion of small concentrations are less likely to cause infection and if it does cause infection is likely to cause asymptomatic infection. The usual concept of an epidemic threshold breaks down. Epidemics can occur even when the classic definition of R_0 is less than 1. The phase transitions in this population are of a hybrid nature, reflecting an underlying saddle-node bifurcation. Two populations with the same number of people and the same total water supply can face very different outcomes with just a small change in the scale at which the water is mixed.

Michele Tizzoni (ISI Foundation, Italy)
Quantifying social contacts in a household setting of rural Kenya using electronic tracking devices
Background: Close proximity interaction between individuals influences how infections spread. Quantifying close contacts in developing world settings, where such data is sparse yet disease burden is high, can provide insight into the design of intervention strategies such as vaccination. Recent technological advances have enabled collection of dynamic face-to-face human contact data using radio frequency proximity-sensors. Methods and findings: The data arise from a prospective study of 5 households in rural Kenya, followed through 3 consecutive days. All residents carried wearable proximity sensors to collect data on their close (<1.5 metres) interactions. Data collection for residents of three households was contemporaneous. We define contact matrices and temporal networks for 75 individuals and patterns by age and time of day in household contact structures. We demonstrate the stability of number and duration of contacts across days. The distribution of contact durations followed a power-law relationship consistent with data from other settings. Within household contacts are mainly among children and between

children and adults, characterized by daily regular peaks in the morning, midday and evening. Intra-household contacts are between adults and more sporadic when measured over several days. Conclusions: Wearable proximity-sensors can be used to objectively collect high resolution temporal data from previously unsampled populations without direct supervision. The methodology and results from this study may be used in design of future studies using similar electronic devices targeting communities, including households and schools, in the developing world setting.

Chiara Poletto (Inserm, France)
Multi-pathogen competition and persistence in a spatially structured environment
The ecology of infectious diseases presents many fascinating dynamical problems for the complexity of interactions characterising host-pathogen systems. I will focus on a central ingredient within this context that is hosts' space structure and mobility. Theoretical models merging metapopulation scheme with network approaches allow a transparent characterisation of how this component shape the phase space of ecological outcomes. I will describe recent results on the dominance/co-dominance between two interacting strains, and on the persistence of a rapidly mutating pathogen. These results highlight general mechanisms at the basis of spatial ecology of pathogens.

Spencer Fox (University of Texas, US)
Strain-transcending immunity and population-level risk for pandemic influenza emergence
Pandemic influenza preparedness currently relies on long-term antiviral stockpiles and intensive year-round worldwide surveillance systems. Understanding population risk for pandemic emergence could allow for more efficient resource allocation and surveillance efforts. The influenza pandemics of recorded history emerged during the influenza off-season (Spring/Summer months), suggesting that seasonal influenza epidemics may constrain the timing of pandemic invasion. Interactions between seasonal and pandemic influenza subtypes could be mediated by a generalized immune response following infection with any one subtype, a conclusion supported by epidemiological and immunological evidence. We model this strain-transcending immunity with a simple two-strain disease transmission network model. Our model is a modified two-strain SIR framework with a protected class that allows for a period of generalized immunity following infection with one strain. We vary disease parameters controlling contact network heterogeneity, epidemic and pandemic transmission and recovery rates, strength and length of strain-transcending immunity, and pandemic strain introduction timing to better understand population susceptibility to pandemic invasion. We find four pandemic introduction regimes: (1) non-overlapping outbreaks, (2) invasion and coexistence with epidemic strain, (3) invasion and displacement of epidemic strain, or (4) complete exclusion of the novel strain. Contact rate heterogeneity is an important determinant of disease regime with low heterogeneity facilitating pandemic invasion, and high heterogeneity allowing for pandemic exclusion. Within exclusion regimes, even mild interference between the seasonal and pandemic influenza can result in drastic reductions in risk of invasion. Our results suggest that even minimal strain-transcending immunity can alter pandemic invasion risk as a function of seasonal epidemic prevalence and timing, and highlight the need to develop a better understanding of strain-transcending immunity to more efficiently prepare for novel influenza introductions in the future.

Laurent Hebert-Dufresne (Santa Fe Institute, US)
Interacting strains on realistically clustered networks: when diseases can benefit from modular contact structure
We investigate the impact of contact structure clustering on the dynamics of multiple diseases interacting through coinfection of a single individual, two problems typically studied independently. We highlight how clustering, which is well-known to hinder propagation of diseases, can actually speed up epidemic propagation in the context of synergistic coinfections if the strength of the coupling matches that of the clustering. We also show that such dynamics lead to a first order transition in endemic states, where small changes in transmissibility of the diseases can lead to explosive outbreaks, and regions where these explosive outbreaks can only happen on clustered networks. We develop a mean-field model of coinfection of two diseases following Susceptible-Infectious-Susceptible dynamics which are allowed to interact on a general class of modular networks. We introduce a criterion based on tertiary infections which yields precise analytical estimates of when clustering will lead to faster propagation than non-clustered networks. This closed form analysis allows us to highlight the impact of disease interactions as a function of the

transmissibility of both diseases and of their respective characteristic time-scales. We also characterize how the spreading patterns of interacting strains differ from that of a single strain. We find that diseases end up being more prevalent within dense communities and that individuals can often require more than a single exposure before infection. These results, akin to the so-called social reinforcement effect found in complex contagions (e.g. spread of behaviours and memes), could potentially lead to novel detection methods for disease interactions based on network theory. Finally, we illustrate how our methods apply to other type of coupling (i.e., parasitic and antagonistic interactions) where we also see that clustering can at times speed up dynamics. However, in the context of interacting diseases, such as HIV with syphilis and pneumococcal pneumonia with influenza or respiratory syncytial virus, our results send a clear message: random networks or mass-action models do not always provide worst-case scenarios.

Patrick Staples (Harvard University, US)
Incorporating Contact Network Structure in Cluster Randomized Trials
Whenever possible, the efficacy of a new treatment, such as a drug or behavioral intervention, is investigated by randomly assigning some individuals to a treatment condition and others to a control condition, and comparing the outcomes between the two groups. Often, when the treatment aims to slow an infectious disease, groups or clusters of individuals are assigned en masse to each treatment arm. The structure of interactions within and between clusters can reduce the power of the trial, i.e. the probability of correctly detecting a real treatment effect. We investigate the relationships among power, within-cluster structure, between-cluster mixing, and infectivity by simulating an infectious process on a collection of clusters. We demonstrate that current power calculations may be conservative for low levels of between-cluster mixing, but failing to account for moderate or high amounts can result in severely underpowered studies. Power also depends on within-cluster network structure for certain kinds of infectious spreading. Infections that spread opportunistically through very highly connected individuals have unpredictable infectious breakouts, which makes it harder to distinguish between random variation and real treatment effects. Our approach can be used before conducting a trial to assess power using network information if it is available, and we demonstrate how empirical data can inform the extent of between-cluster mixing.

Nathaniel Hupert (Cornell University, US)
Complexity in Contagion Response
Models that capture complex features of transmission dynamics have been successful in generating insights into how diseases may spread, but not necessarily into how to stop them from spreading, or what consequences their spread may hold for health systems that are responsible for public safety. Health officials, who increasingly look to quantitative models for insight into how to optimize their response strategies, may fail to appropriately use model outputs if they find inadequate representation of the complexity of their daily jobs in modeled response options. This talk will consider complicated and complex features of public health and medical response to contagion, with illustrations from the health care system in New York City.

James Koopman (University of Michigan, US)
Polio Eradication Modeling for Crucial Endgame Decisions
Empirical success of eradication efforts in Latin America motivated the World Health Assembly to endorse polio eradication efforts in 1988 with a goal of eradication by 2000. Modeling played no role and was eschewed by polio eradication leaders. Now, 15 years past the original goal, a purely empirical basis is clearly insufficient. Never before have high transmission areas been in a state where lack of high level transmission has stopped the regular boosts of immunity that come from recurrent polio virus exposures. Moreover there is almost no empirical base of poliovirus infection studies. Almost all data is based on poliomyelitis surveillance and poliomyelitis cases are a tiny fraction of all poliovirus infections. None-the-less a largely empirically based plan to stop the use of oral polio vaccines under the presumption that three years without a polio case is sufficient to insure there is no ongoing silent circulation. No vaccination of adults whose waned immunity allows them to carry on chains of transmission is being considered. Since 2000 Kid Risk Inc. has published 45 modeling papers that have played a role in guiding eradication policies. Groups at Imperial College and the Institute for Disease Modeling have also made valuable contributions. Our University

of Michigan group became concerned about the formulation of waning immunity in the models being used and began examining polio eradication in an alternative framework. But a community of modelers that builds on the work of each other, shares code and data, and collaboratively or contentiously works toward identifying key problems in work performed to date has not emerged. One of the major impediments has been the lack of data accessibility from the polio eradication efforts. The difficulty in the approaches of the main modeling groups to relate to each other's work has been another impediment. The Center for Inference and Dynamics of Infectious Diseases (CIDID) organized a workshop of all the modeling groups for July 1&2 in the hopes rectifying this situation. In this presentation we will review the outcome of this workshop and the reaction to the following piece of work presented by University of Michigan investigators: Stopping oral polio vaccination (OPV) when polio virus transmission still exists could lead to augmented transmission that could set back polio eradication efforts. To help inform decisions about stopping OPV, we perform a model based analysis of the impact of waning immunity, the extent and timing of vaccination, and the transmission of wild polio viruses (WPV) and OPV on prolonged silent circulation after the last paralytic poliomyelitis case is observed. The vaccination ramp-up time between the beginning of vaccination and finally achieving a level of vaccination that leads to the disappearance of paralytic polio cases plays a key role in amplifying the interaction between waning immunity and high rates of transmission in a population in causing prolonged silent circulation. Long ramp up times in high transmission settings cause effective reproduction numbers to stay just under 1 and thus not drive WPV prevalence down enough to cause eradication after poliomyelitis cases disappear. Waning immunity over long ramp-up times increases transmissions from reinfected individuals who help sustain silent circulation. India, and the remaining endemic countries have conditions generating these interactions whereas in places where eradication occurred previously, the ramp-up time was not long enough. The resulting silent circulation has low prevalence and is likely to go undetected. Whether these conditions exist currently, and whether vaccinating adults in the final OPV rounds in places with these conditions would put an end to silent circulation deserves assessment by fitting models to diverse data that has been collected but is not generally available.

Sergio Arregui (University of Zaragoza, Spain)

Efficacy measurement and impact evaluation for Tuberculosis new vaccines

Tuberculosis is still one of the deadliest infectious diseases, being yet responsible for a million and a half deaths per year all around the world . The situation is specially dramatic in developing countries of Africa and Asia. The necessity of develop mathematical models that could help to control or eradicate the disease is beyond doubt. However, the task is not an easy one to handle. The pathogen causing the disease, Mycobacterium Tuberculosis, presents a very complex life cycle. After infection, sometimes it causes the disease in a relatively short time, while in other cases it enters in a dormancy state, without causing the disease, during many years until it is activated and the disease proliferates. This brings the need to tackle very diverse time scales for a proper modeling, as well as the heterogeneity in the host responses –that seems to be strongly correlated with the age–. Any attempt to quantify the spreading of the disease will need to introduce new ingredients, according to these challenges that in many cases surpass the assumptions of the classical mathematical epidemiology, such as age-dependent contacts, the evolution of demography or the non-stationarity of initial conditions. At the level of clinical research there are also some challenges to overcome. Current BCG (Bacillus of Calmette-Guerin) vaccine has proved to be unable to stop the proliferation of the disease, therefore in order to approach the major health issue that Tuberculosis represents, tens of new vaccine candidates are under development at this moment. These vaccines bestow different mechanisms of protection and are designed to be administered at different ages. They could affect different stages of the Natural History of the disease, or they could be affected by different effects that decrease their efficacies –blocking, masking, etc.– Definitely, vaccines add additional complexity to the problem. A correct quantification of the impact a vaccine can provide, and more useful, a comparison between different vaccines and strategies, need a rigorous exploration of this landscape of possibilities. Not only that, but all these nuances also play a role in the performance of the clinical trials. As correlates of protection for Tuberculosis are still unknown, randomized trials are essential to determine the efficacy of each vaccine. This heterogeneity in the behaviour of the different possible vaccines – in close relation with the intrinsic complexity of the life cycle of the bacterium– has relevance in different features of the clinical trials, such as sample size calculations or the statistical power provided. A correct parametrization of the effect of a vaccine through clinical trials is imperative to a posterior evaluation of its impact in a population using epidemiological models. In this work we uncover the different consequences triggered by the variability of protection mechanisms of different vaccines, in the determination of the efficacy of the vaccines with clinical trials – using stochastic models– and also in the evaluation of the impact of those vaccines –through spreading models, that take into account this new complexity: age-related contacts, evolution of demography–. We will see for

instance that the more or less accepted fact that the higher impact is obtained with adolescents-focused vaccines could be compromised if these other effects and additional dimensionality play a major role.

Eben du Toit (University of Pretoria, South Africa)
A control systems methodology for intervention in the spread of diseases on networks
Contact networks are fundamental for the analysis of the spread of diseases. The field of control systems complement this analysis by proposing methods to compare various intervention strategies. Selective pinning control of the average transmissibility in a contact network needs only about half the control action to reach the same epidemic outcomes compared to controlling all nodes of the network. Complete intervention (all nodes pinned) is the public health norm. Where budget is a constraint, the concept of the QALY can be controlled in networks. Quality-functions can realistically be constructed and the budget optimally controlled through the use of non-linear model-predictive control. A comparison is given of all such control strategies researched so far. Predictive control is roughly 6% more resource-efficient in the use of medicine doses for the random exponential-power-law networks proposed, compared to proportional feedback control. Simulation results are compared for networks up to N=10000 nodes.

Shweta Bansal (Georgetown University, US)
Inferring livestock contact and infectious disease dynamics across scales
Transportation of livestock carries the risk of spreading foreign animal diseases throughout a susceptible population, leading to costly public and private sector expenditures on disease containment and eradication. Individual animal tracing systems that exist in countries other than the US have allowed epidemiologists and veterinarians in those countries to model the risks engendered by livestock movement and prepare responses designed to protect the livestock industry. Within the US, data on livestock movement is not sufficient for direct parameterization of disease models, but network models that assimilate limited data provide a path forward in model development to inform preparedness for emerging and endemic livestock disease outbreaks.

Gianluigi Rossi (IZSER, Italy)
The effect of direct and indirect contacts on potential epidemic spread among the dairy farms network in the Province of Parma (Emilia-Romagna, IT)
Although live animals exchange is considered the most effective route of disease transmission between farms, the spread through contaminated equipment, vehicles, or personnel proved to be crucial for many epidemics, included the 2001 foot-and-mouth disease in the UK or the worldwide spread of avian flu in 2000s decade. Among farm professional visitors, veterinarians are considered particularly dangerous for disease spread due to their close contact with animals. While between-farm direct contacts (i.e. animals exchange) have been studied in depth over the past 20 years, indirect contacts (e.g. through veterinarians or other operators) have been often overlooked, mainly because of the challenging task represented by data retrieval. Our work aims to understand the role of indirect contacts due to veterinarians' visits in a potential epidemic spread. Starting from 1349 dairy farms of the Italian Province of Parma, we build two contact networks using data on cattle movements (direct contacts), veterinary officers and practitioners (indirect contacts). Firstly, we employ network analysis techniques to compare the general network structure of the considered routes of transmission. Moreover, we compared the farms acting as a super-spreader in the direct contact network vs. the indirect one, and we analysed the effect of the two transmission routes combined. Finally, we validated the observed contact networks using data on Johne's disease, currently endemic within the area. Direct and indirect networks showed non-trivial differences, with veterinarian visits creating more connected networks than cattle movements. Moreover, the analysis on super-spreaders showed that the ones defined with respect to the two transmission route (direct vs. indirect) were totally different. This is important in particular for measures such as targeted surveillance and control. Moreover, the two routes of transmission combined, showed a potential spread capacity higher than just the sum of the two. The validation with Johne's disease data showed that veterinarian visits contacts were more important at a spatial scale such as the provincial one, while animal movement were determinant at broader spatial scales, such as the regional one. In conclusion our works highlighted the relevance of indirect contact in the potential epidemic spread, in particular at local spatial scale. This phenomenon showed a total independence with respect to direct contacts, suggesting that it needs to be treated separately.

Enys Mones (Technical University of Denmark)
Epidemic Monitoring in Complex Social Systems
Social systems—densely connected populations—are complex with respect to their structure and dynamics they display. The complexity of social interactions is caused by people communicating on multiple channels and effortlessly switching between them. At the same time, the choice of the communication channel is often not random and may depend on the desired intimacy, place, time, and many other contextual factors. Understanding the high-resolution structure of such complex social systems is important for devising public health policies, especially around monitoring and containing epidemic outbreaks. An important question, that has gained increased attention in the last years, is how to learn about epidemic outbreak in the population before this outbreak becomes large. This can be achieved by monitoring a relatively small number of chosen individuals, in the, so called, targeted monitoring. Despite a significant progress in studying social systems, majority of our understanding has been so far limited to probing single communication channels. As a result, little is known how these multiple channels describe different epidemiological properties of a social system. This is not only of fundamental interest of how to properly study social fabric, but also has very practical potential implications. Since not all the channels are equally easy to collect, with Big Data channels already existing in a database somewhere, understanding how different channels can help us in epidemiology may make a difference between theoretical and practical. Here we take a peek into a complex social system of few hundred individuals through—for the first time at scale—multiple communication channels in order to understand how the multiple channels are useful for network epidemiology, specifically for targeted monitoring. We show that the structure and dynamics revealed by various channels differ significantly. However, individuals important for outbreak monitoring can be identified from Facebook and call networks, channels significantly easier to collect than full close-proximity network. Surprisingly, these channels do not simply identify individuals most central in the close proximity network, but extract the social core of the system—individuals with most spreading power during social times. The usefulness of Big Data channels (Facebook and call metadata) for the epidemic monitoring constitutes a directly actionable result. Our results indicate also that the way different communication channels reflect the underlaying social system is non-trivial. Thus, in order to fully understand social fabric, it is important to collect information cutting across multiple communication channels.

Glenn Lawyer (Max Planck Institute for Informatics)
Predicting the Spreading Power of Infectious Nodes in Temporal Networks
Epidemiology, and the study of spreading processes in general, increasingly relies on network models due to their ability to express the heterogeneity in contact structures. As the field matures, the importance of temporal structure is increasingly recognized. Recent work shows that considering the continuous time evolution of spread allows the quantification of the influence of every node in the network. In this work we evaluate the method computing the expected force (ExF) of infection generated by each node in a temporal setting, compared to the previously evaluated static case. We first measure the stability of this metric over time. Then we explore relationship between a summary of node ExF and how quickly an epidemic seeded from the given node saturates the network under a Susceptible-Infected (SI) model. The results show that the predictive power of ExF is also high in the temporal setting and outperforms other evaluated approaches.

*for complete authorship please refer to CCS app.