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Investigating spatiotemporal dynamics and synchrony of influenza epidemics in Australia: An agent-based modelling approach

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ABSTRACT

In this paper we present ACEMod, an agent-based modelling framework for studying influenza epidemics in Australia. The simulator is designed to analyse the spatiotemporal spread of contagion and influenza spatial synchrony across the nation. The individual-based epidemiological model accounts for mobility (worker and student commuting) patterns and human interactions derived from the 2006 Australian census and other national data sources. The high-precision simulation comprises 19.8 million stochastically generated software agents and traces the dynamics of influenza viral infection and transmission at several scales. Using this approach, we are able to synthesise epidemics in Australia with varying outbreak locations and severity. For each scenario, we investigate the spatiotemporal profiles of these epidemics, both qualitatively and quantitatively, via incidence curves, prevalence choropleths, and epidemic synchrony. This analysis exemplifies the nature of influenza pandemics within Australia and facilitates future planning of effective intervention, mitigation and crisis management strategies.

1. Introduction

Early recognition and curtailing of outbreaks of infectious diseases is crucial to policy making and public health. Without efficient intervention, international travel can result in the spread of highly infectious pathogens around the globe within weeks of the initiation of the outbreak, as evidenced by the 2009 H1N1 (swine flu) pandemic. Moreover, infectious diseases are large burdens on the economy. For instance, a 2007 study estimated that the annual cost of seasonal influenza to the health system in Australia was AU $828-884 million [1]. Effective strategies for mitigating outbreaks should include a suitable combination of immunisation, vaccination, and palliative care [2–4] and planning these strategies requires reliable forecasting through simulation of various ”what if?” scenarios. Without efficient intervention, highly infectious pathogens, such as swine flu, result in international travel carrying the virus around the globe within weeks to months of the initiation of the outbreak, causing a worldwide public health emergency [5–8].

Intergration of large-scale datasets and explicit simulations of entire populations down to the scale of single individuals has considerably improved the accuracy of epidemiological models [9]. Furthermore, an effective intervention requires not only an accurate modelling and surveillance of the disease dynamics, but also implementation of the underlying contact networks and their topologies. This requires a detailed theoretical and practical understanding of the interplay between epidemic processes, mobility

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patterns (especially over long distances), and population data. By running multiple computer simulations while varying the sources of infection, we can then ascertain the average social and health impact, as well as "zoom in" on specific pathways and patterns of epidemics.

While there are currently many useful models and tools to assist in the analysis and prediction of contagion processes, none are adequate in terms of precise and integrated tracking, predicting and mitigating epidemics at the national-level for Australia. It remains a challenge to generate and simulate a realistic and dynamic contact network, accounting for both mobility and human interactions representing the demographics of Australia through an individual-based epidemiological model. Moreover, as evidenced by Cauchemez et al. [10], modeling the transmission of respiratory diseases must specifically account for structuring of schools, grades, and classes due to the "back-and-forth waves of transmission between the school, the community, and the household." These challenges are particularly important for investigating epidemics in Australia, where the population is concentrated mainly around urban areas.

We have addressed this need by developing ACEMod, the *Australian Census-based Epidemic Model* that employs a discrete-time and stochastic agent-based model to investigate complex outbreak scenarios at various spatiotemporal levels. The simulator comprises 19.8 million software agents where each agent contains a set of attributes of an anonymous individual. The agents are generated such that the distributions at multiple scales concur with key demographic statistics of the 2006 Australian census data. The next layer of the model includes mobility patterns (with respect to work, study and other activities) in order to characterise potential interactions between spatially distributed agents. The final layer describes local transmission dynamics by combining agent health characteristics, such as susceptibility and immunity to diseases, with a natural history model for influenza. The simulation runs in 12 hour cycles ("day" and "night") over the course of an epidemic such that agents interact in different social mixing groups depending on the cycle. Given a surrogate population generated in this way, we run multiple instances of each scenario, varying the disease infectiousness and outbreak locations to give insight into the spread of influenza pandemics around Australia.

The novel aspects of AceMod include (i) the spatial fidelity of the stochastically generated population, calibrated to Australian Census and the Australian Bureau of Statistics (ABS) datasets that utilise multi-scale distributions over school data and hierarchical mixing groups; (ii) its refined models for the transmission and natural history of the simulated infection, based on the latest available epidemiological studies; and (iii) the focus on measures of spatiotemporal complexity of influenza epidemics.

We evaluate the spread of influenza in space and time through Australia via incidence curves, prevalence choropleths, and epidemic synchrony. Incidence curves characterise the disease by plotting the number of newly *ill* individuals (i.e., the incidence) at each time step. Here, ill refers to infected agents that are showing symptoms. This illustrates the severity of the disease over time and can be used to compare different pathogens or mitigation strategies. Then, in order to qualitatively study the evolving spatial distribution of the epidemic over time, we record the percentage of ill individuals (i.e., the prevalence) in each community at a given time step and give snapshots of this distribution through choropleths taken at key times of the epidemic. Finally, we examine spatial hierarchies in disease prevalence by analysing the variance in the timing of the epidemic peaks in each community (i.e., the synchrony). The spatiotemporal synchrony of disease spread between communities correlates to the size of the communities, suggesting the disease transmission is more associated with social connectivity rather than geographic distance.

2. Related work

Well-established stochastic models of epidemics often use SIR and SEIR differential equations for the population dynamics of susceptible (S), exposed (E), infectious (I), and removed/recovered (R) individuals [11]. While these models are suitable for analysing the general behaviour of an epidemic on larger scales, with a focus on global variables, they do not allow us to make accurate predictions at a finer resolution.

In many scenarios it is beneficial to trace the dynamics in a more fine-grained way especially during the initial or final stages of an outbreak, when person-to-person transmission processes dominate [12]. As a result, stochastic agent-based discrete-time simulation models were developed to capture how the uncertainty in disease diffusion varies in different social groups and affects the overall analysis and predictions of epidemics [5,12]. These models have been used to assess vaccination and antiviral prophylaxis strategies on a local level, highlighting importance of detailed modelling of contact patterns [12–14]. These models further allow us to investigate strategies at large-scale regional and national levels for containing an emerging pandemic influenza strain at its source [5,6].

Early efforts include an agent-based simulation by Elveback et al., where they modeled a small artificial population to represent a community and defined multiple contexts in which individuals interact, in order to explore the disease spread. Later works [5,12] leveraged increased computational power to further this methodology, considering populations on a larger scale based on exact census data. A suite of scalable agent-based modelling software simulators was described in a series of papers[15–19]. Simdemics was designed as a general purpose simulation environment supporting 300 million agents, aimed at modelling pandemic planning and response to a range of crisis scenarios, such as H1N1/H5N1 pandemics and bio-terrorism events [18]. A number of simulators were built upon Simdemics framework. For example, a high-performance computing modelling environment, EpiSims, designed as a distributed discrete event simulator, modelled disease transmission via sub-groups of people in a given location. The location objects were distributed across CPUs and people objects moved among locations, using various census, land-use and population-mobility data. It has been successfully applied to modelling of smallpox [15] and pandemic influenza plan [20]. The EpiSimdemics algorithm [16,19] was based on contagion diffusion across a person-location graph, a bipartite graph where the nodes represented people and locations, while the edges indicated a person's presence at a location. A person-location graph of the entire population of the United States included 300 million nodes (people) and 1.5 billion edges, and ran on the 352,000 core NCSA BlueWaters system, so that 120