



An agent-based model driven by tropical rainfall to understand the spatio-temporal heterogeneity of a chikungunya outbreak



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ARTICLE INFO

Article history:

Available online 16 August 2013

Keywords:

Agent-based model
Asymptomatic
Chikungunya
Computational epidemiology
Spatio-temporal
Urban scale-free network

ABSTRACT

Vector-borne diseases, such as dengue, malaria and chikungunya, are increasing across their traditional ranges and continuing to infiltrate new, previously unaffected, regions. The spatio-temporal evolution of these diseases is determined by the interaction of the host and vector, which is strongly dependent on social structures and mobility patterns. We develop an agent-based model (ABM), in which each individual is explicitly represented and vector populations are linked to precipitation estimates in a tropical setting. The model is implemented on both scale-free and regular networks. The spatio-temporal transmission of chikungunya is analysed and the presence of asymptomatic silent spreaders within the population is investigated in the context of implementing travel restrictions during an outbreak. Preventing the movement of symptomatic individuals is found to be an insufficient mechanism to halt the spread of the disease, which can be readily carried to neighbouring nodes via sub-clinical individuals. Furthermore, the impact of topology structure vs. precipitation levels is assessed and precipitation is found to be the dominant factor driving spatio-temporal transmission.

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1. Introduction

The emergence and persistence of human pathogens in the environment represents a constant threat to society, with global implications for human health, economies and ecosystems. Of particular concern are vector-borne diseases, such as dengue, malaria and chikungunya, whose incidence is rapidly increasing across their traditional ranges and, more alarmingly, infiltrating previously unaffected areas. This unprecedented situation has been partly attributed to the increase in global temperatures in recent decades which has allowed non-native mosquito species to invade new territories and successfully colonise previously inhospitable environments (Bernstein et al., 2007). This has led to a surge in the incidence of mosquito-borne diseases in previously unaffected areas and a heightened threat of further more severe outbreaks (Tabachnick, 2010). Local transmission of these traditionally tropical diseases has even been recorded on the European continent in recent years (Gould et al., 2010; La Ruche et al., 2010; Schmidt-Chanasit et al., 2010; Andriopoulos et al., 2012). Of particular concern is the possible reemergence of malaria, which is one of the deadliest vector-borne diseases in the world, with approximately

half of the global population currently at risk. Malaria was eradicated from Europe in 1975. However, the current continent-wide increase in imported cases, the permanent presence of a highly suitable vector (*Anopheles atroparvus*), and the recently recorded autochthonous transmission in Greece (Andriopoulos et al., 2012) highlights the constant threat it poses in temperate climates. Historically, diagnosed cases of dengue fever in Europe were imported by overseas travellers. However, local transmission has been documented in recent years in France, Croatia and Madeira (La Ruche et al., 2010; Schmidt-Chanasit et al., 2010; Sousa et al., 2012). The principal disease vector in tropical regions is the mosquito *Aedes aegypti*. However, the introduction and subsequent spread of the Asian tiger mosquito (*Aedes albopictus*) into temperate regions has provided a highly competent vector carrier (Semenza and Menne, 2009) and has increased the threat of local dengue transmission. This mosquito has been linked to the local dengue transmission recorded in Europe (La Ruche et al., 2010; Schmidt-Chanasit et al., 2010). It can act as a vector for several tropical diseases, including chikungunya, and was the cause of the first large outbreak of chikungunya recorded in a temperate region in North-Eastern Italy in 2007 (Rezza et al., 2007). Furthermore, the European Centre for Disease Control (ECDC) has just recently recorded established populations of the classic dengue vector *A. aegypti* within Europe (Medlock et al., 2012). Public health authorities with little or no experience with such diseases need to rapidly put preparedness plans in place in advance of future outbreaks and understanding the dynamics of the diseases and the viability of proposed control strategies is of paramount importance. The dynamics of

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vector-borne diseases are determined by the interaction of the host and vector populations, in addition to the characteristics of the infectious agent itself. Mathematical models have been implemented to describe the spread of these infections and their temporal dynamics are well documented (Fischer and Halstead, 1970; Dumont et al., 2008; Moulay et al., 2011; Dietz et al., 1974). However, their spatial spread has received less attention. In particular, the importance of heterogeneities in human population structures has been highlighted (Smith et al., 2004), although their impact has not been fully assessed.

Several modelling approaches are possible to describe interacting populations in spatial heterogeneous environments. Deterministic models have been implemented in the form of reaction–diffusion equations describing the random movements of individuals within populations (Murray et al., 1986; Noble, 1974; Pech and McIlroy, 1990). Metapopulation or patch models can be employed to group populations into residents and visitors (Sattenspiel and Dietz, 1995; Arino and Van den Driessche, 2003; Keeling and Rohani, 2002) and the force of infection will depend on infected individuals in both home and foreign patches. Network models have also been described where each individual has a unique force of infection determined by the number of connections with infectious contacts (Keeling and Eames, 2005; Ben-Zion et al., 2010). Adaptive social networks have also been explored where susceptible individuals are able to disconnect from infected individuals (Gross et al., 2006). More recently, agent-based models (ABMs), also known as individual-based models, where each individual is explicitly represented and characterised, have become a powerful tool to describe disease spread through heterogeneous populations. Such models have been implemented to describe the spread of smallpox (Halloran et al., 2002), hepatitis (Ajelli and Merler, 2009) and influenza (Ferguson et al., 2005) and, in particular, dengue (Favier et al., 2005b; Focks et al., 1995; Isidoro et al., 2011) and malaria (Gu et al., 2003). ABMs have proved to be particularly useful when assessing the impact of infection control strategies (Ferguson et al., 2005). They provide the ability to manipulate individual level contact rates and offer the advantage of being able to analyse spatially focused interventions. The rapid global spread of pandemic influenza H1N1 and severe acute respiratory syndrome (SARS) has highlighted the need to assess how heterogeneous social structures can impact the speed and efficiency at which human pathogens propagate through modern populations. The restriction of travel during the H1N1 and SARS outbreaks has been analysed (Riley et al., 2003; degli Atti et al., 2008). However, the impact of asymptomatic individuals was not considered in these studies. This issue is particularly important for vector-borne diseases, as asymptomatic individuals will, presumably, be equally infectious to the biting mosquito as symptomatic individuals. This is in contrast to respiratory diseases such as influenza, where symptomatic individuals transmit the infection more readily due to physical signs of illness (coughing, sneezing, etc.). The issue of asymptomatic transmission and the restriction of travel has not previously been assessed for vector-borne diseases using an ABM approach. While ABMs are computationally expensive and their scope can be limited by the population size, they provide an unparalleled level of detail which is a vital component of mosquito-borne diseases as mosquito populations are intrinsically coupled to the local human population size, availability of breeding sites as well as human behaviour. Intervention measures to control these diseases are primarily based on mosquito reduction efforts. Therefore, a successful intervention requires knowledge of localised spatial structures and the mobility of the host population. These details are overlooked by large scale models for the spatio-temporal evolution of disease transmission and ABMs allow the constrictive nature of the homogeneous mixing assumption to be overcome.

The methodology presented in this paper focuses on the dynamics of chikungunya as it is not burdened with the complications of multiple strains or causative parasites, which is inherent in other disease models such as dengue or malaria. However, the proposed concepts and models can be readily adapted to successfully describe other vector-borne diseases. The chikungunya virus is an acute febrile illness which was first isolated in 1953 in Tanzania (Pialoux et al., 2007) and is primarily transmitted by the *A. aegypti* mosquito. In humans, the disease usually manifests as a fever, skin rash and arthralgia. Following sporadic outbreaks in Africa and Asia, a large outbreak started in Kenya in 2004 and spread to the islands of the Indian Ocean in 2005 (Staples et al., 2009). On the island of La Réunion, the virus was transmitted by a secondary vector, the *A. albopictus*, which was also responsible for the outbreak in Italy in 2007 (Rezza et al., 2007). This outbreak was particularly significant because it represented the emergence of a new viral mutation (Schwartz and Albert, 2010) that infected over one third of the island population (Renault et al., 2007).

In this paper we formulate an agent-based model (ABM) to investigate the spatio-temporal heterogeneity of an infectious vector-borne disease outbreak. We use this model to explore the impact of precipitation-dependent vector populations and the structure of the underlying network topology on the epidemiological dynamics. We use chikungunya as an example. In order to realistically reproduce the setting of a chikungunya outbreak, we drive an ABM with 2 years of daily precipitation data for La Réunion, where a chikungunya outbreak occurred between 28 March 2005 and 12 February 2006 (Medlock et al., 2012). A direct comparison between the simulated epidemic and the La Réunion outbreak is not possible without detailed demographic and transportation data. Furthermore, the La Réunion outbreak was unique in that a second wave resulted from a viral mutation, an effect not considered in the model presented herein. The methodology, structure and implementation of the ABM are presented in Section 2. The ABM has a broad scope and, in its current form, can be applied to any single-strain vector-borne disease. However, chikungunya fever is chosen as the illustrative disease to demonstrate the model's capabilities. The movement and clinical status of infected individuals is analysed in Section 3. In particular, the impact of restricting the movement of symptomatic cases is considered and discussed in the context of a public health intervention to control the spread of the disease.

2. Methods

2.1. Agent-based model

2.1.1. The urban network and agents

The model is an agent-based model (ABM) implemented as an 'urban network' where *host agents* 'live' in the network's nodes, which can be thought of as villages, towns or cites. The host agents are allowed to travel to their neighbouring nodes, thus mimicking the travel of individuals within an area where a number of villages and cities are located. The nodes are connected by *links*, which represent transportation channels such as roads and highways.

A *scale-free* network (Fig. 1) has been used, as it is commonly believed that many natural and (human) social networks follow such a topology (Pastor-Satorras and Vespignani, 2001; Albert and Jeong, 1999; Barabási, 2002). As a comparison, a regular network has also been used where a Von Neumann four-links-per-node neighbourhood structure is implemented (Wolfram, 1983), except in the border nodes where three and two-links per-node were used.

Each node/village of the network accommodates a number of host agents, which is proportional to both the number of connections in their node/village and a random number, say x , drawn from

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