

Large-scale Epidemiological Modelling: Exploring the Impact of the ASEAN Economic Corridors Policy on the Dengue Fever Epidemic

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In this study, we present an implementation of a hybrid, integrated model that supports various explorations of the relationship between the increasing regional integration among ASEAN countries and the Dengue fever epidemic in the same countries. Using the available public data on economic exchanges, climatic conditions and dengue fever cases as the input, we designed a complex model composed of three sub-models: a SEIR/SIR mathematical epidemiological model that operates at a local scale and combines the population dynamics of mosquitoes with the computation of infected mosquitoes and people, a cellular automata model that provides support for the spread of infected mosquitoes and people between its cells, an agent-based model based on accurate GIS road data, which reproduces the traffic of trucks between countries, and an agent-based model of control policy decision-making at the scale of each country. All these models were coupled within the same framework, supported by the GAMA modelling and simulation platform (<http://gama-platform.org>), which scheduled them using a timescale of 12 hours over 10 years (from 2002 to 2011). This integrated model has been designed to be completely generic: provided the required data (on climate conditions, dengue cases, commercial exchanges, and health policies) was available, it could be applied to any geographic location at any spatial scale. It has been extensively tested on a specific case study: the terrestrial East-West Economic Corridor, a continuous land route that links Vietnam, Laos, Thailand and Myanmar.

INTRODUCTION

Economic corridors refer to transport networks that support and facilitate the movement of goods, services and people within and between countries. They are one of the most visible consequences of the regional integration impelled by ASEAN member countries since the mid-1990s. In particular, investments in cross-border road projects have paved the way for the development of three terrestrial corridors under the Greater Mekong Subregion (GMS) program, the most important of which is the East-West Economic Corridor (EWEC), which runs from Vietnam, through Laos and Thailand, to Myanmar, representing the only continuous land route that connects the South China Sea and the Andaman Sea in the Indian Ocean. While the implementation of these corridors has had indisputable positive effects on the economic growth of the region, it is also suspected to have fostered undesirable social and environmental consequences, such as the trafficking of people, the incidence of road accidents and the spread of diseases.

In particular, thanks to the availability of public data (between 2002 and 2010 in Figure 1), a significant correlation was observed between the development of trade and tourism among ASEAN countries and the number of dengue fever cases reported each year. Since this disease is a major burden in the region, any hint of a possible relationship between the two phenomena could be critical for policy makers to make informed decisions and design coordinated control policies.

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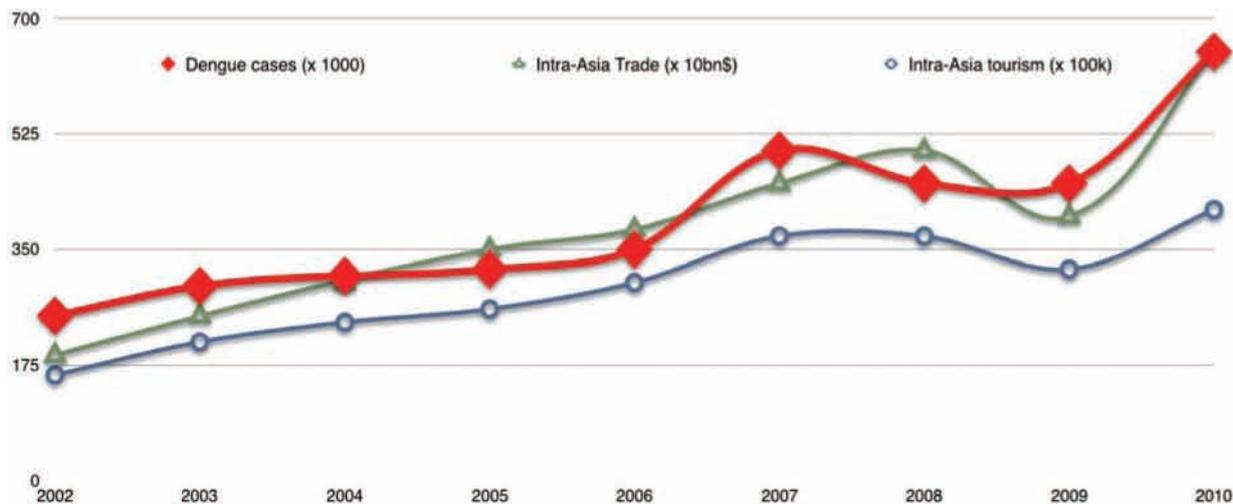


Figure 1. Correlation between the number of dengue cases reported in ASEAN countries (in red) and the trade and touristic exchanges between these countries (in green and blue) between 2002 and 2010.

As a matter of fact, dengue fever is a disease which has an important incidence in Asia: 75% of the world-wide population exposed to dengue fever live in this area (Murray *et al.*, 2013). In ASEAN, the number of cases has increased year after year over the last 10 years. Dengue is a vector-borne disease, which means that its spread is only possible thanks to a vector, in this case, by two different mosquito species: *Aedes albopictus* (a rural mosquito species) and *Aedes aegypti* (an urban mosquito species). When infected mosquitoes bite a susceptible human being, they have a probability to infect him or her. Infected human beings being bitten by a susceptible mosquito may in turn, infect it too.

The symptoms of dengue fever last for 2 to 7 days. The real problem in severe dengue cases is the dengue shock syndrome which happens in 30% of cases and is lethal in 20% of the cases. As 90% of the severe dengue cases affect children under 15 years of age (Malavige *et al.*, 2004), it has become a growing concern for public health policies.

METHODOLOGY

We explored the possibility of a causal relationship behind the correlation described above by implementing a data-driven, large-scale, spatially explicit, integrated model using the GAMA platform (Grignard *et al.*, 2013), in the growing trend of virtual epidemiology (Amouroux *et al.*, 2008). Based on GIS, economic, climatic and population data, the model coupled a local mathematical model of dengue fever dynamics, a mesoscale cellular automaton model of its spread, and an agent-based model of mobility along the EWEC corridor. Only a subset of this integrated model is detailed here. For more details, readers can refer to (Philippon *et al.*, 2016).

Data Collection

Building this integrated model required gathering realistic economical, epidemiological, meteorological, geographical data but also data about the different health policies used in each country. Economic figures (i.e. exportation in dollars from each country to the others, available on the websites of their ministries of trade) were converted into the number of trucks passing through the borders, by attributing an average and somewhat arbitrary value in dollars to each truck (we used the average value for a truck in the US, obtained from the US Department of Transportation website). Epidemiological data were provided by the ministries of health and contained the number of cases recorded by province, by month and by year. We used the incidence of dengue fever as of January 2004 to initialise the model. The meteorological data were obtained from the website <http://climate-data.org>. This website provides information about different meteorological stations, keeping monthly records of temperature and rainfall.

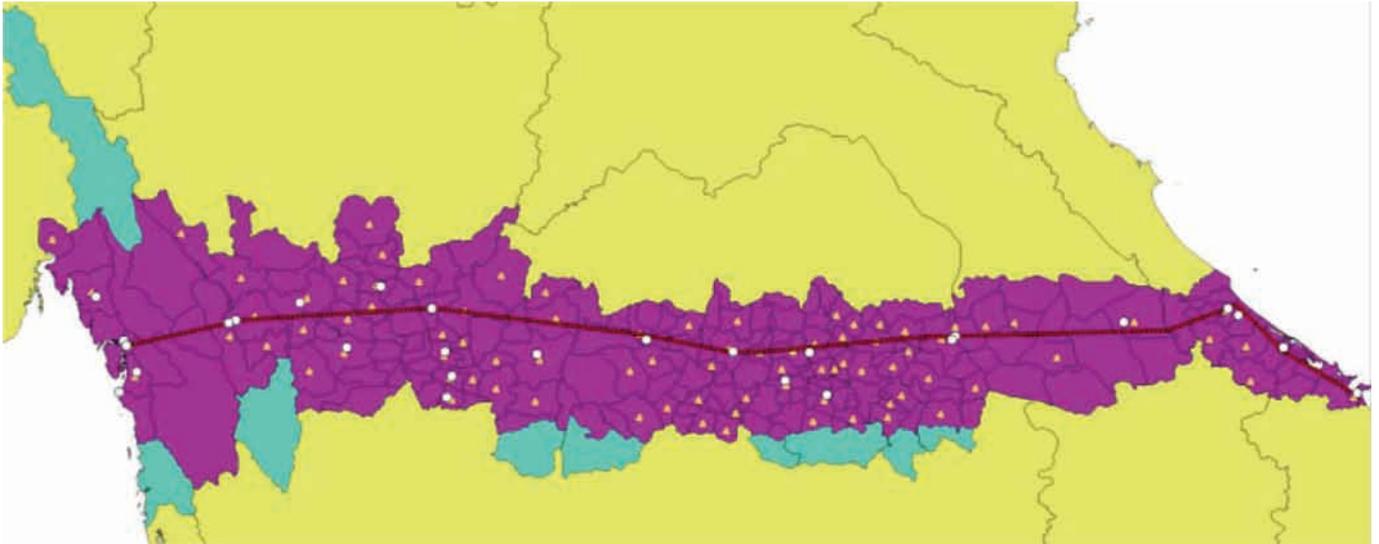


Figure 2. Geographical representation of the Corridor with countries (yellow), provinces (green), districts (purple), cities (circles), weather stations (triangles) and the road.

The geographical shapefile data of the four countries, with their provinces, districts, cities and roads making up the EWEC corridor were obtained from the OpenStreetMap website. They cover an area of 1500km by 400km (Figure 2).

Finally, the data about the health and control policies of the four countries were more qualitative: they came from different articles and studies (mainly Community Based Dengue Vector Control, Lloyd *et al.*, 2013). We have estimated the budget allocated by each country for health policies considering the budget for public health policies, and the factors on which the policies would have an impact (emergence, population of adult mosquitoes, probability of transmission and number of bites per day).



Figure 3. The GIS data used and its coverage with a regular lattice of “cell agents”, composing of a cellular automaton

The main and most important part of the model was a hybrid of a cellular automaton and an agent-based model: a regular grid, composed of “cell agents” was applied to the GIS data (see Figure 3) that supported four processes: (1) the computation of local climatic conditions, (2) the population dynamics of mosquitoes, (3) the transmission of the virus between mosquitoes and humans, and (4) the geographical spread of mosquitoes.

We chose a compartmental Ordinary Differential Equations (ODE) model to represent the disease dynamics based on the model proposed by Manore *et al.*, 2015. It was composed of two populations, mosquitoes and human beings (cf. Figure 5). Human beings could be in four states (Susceptible, Exposed, Infected and Recovered). Mosquitoes could be only in three states (Susceptible, Exposed and Infected) as they could not recover.

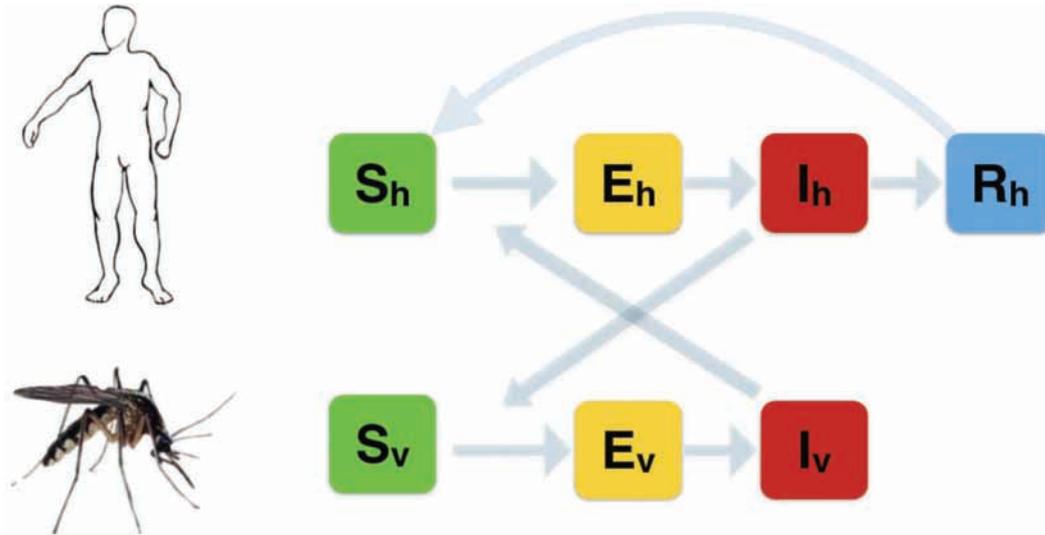


Figure 5. SEIRS-SEI compartment model of dengue transmission dynamics between human beings and mosquitoes

The evolution of this model was described using the following ODE systems (left column for the mosquito population, right column for the human population):

$$\begin{aligned} \frac{dS_v}{dt} &= h_v(S_v + E_v, t) - \lambda_v(t)S_v - \mu_v S_v & \frac{dS_h}{dt} &= \lambda_h(t)S_h + w_h R_h \\ \frac{dE_v}{dt} &= \lambda_v(t)S_v - v_v E_v - \mu_v E_v & \frac{dE_h}{dt} &= \lambda_h(t)S_h - v_h E_h \\ \frac{dI_v}{dt} &= h_v(I_v, t) + v_v E_v - \mu_v I_v & \frac{dI_h}{dt} &= v_h E_h - \gamma_h I_h \\ & & \frac{dR_h}{dt} &= \gamma_h I_h - w_h R_h \end{aligned}$$

with: $\lambda_v(t)$ (resp. $\lambda_h(t)$) as the transfer rate from Susceptible to Exposed for the vector (resp. human beings), v_v (resp. v_h) as the transfer rate from Exposed to Infected for vectors (resp. human beings). γ_h (resp. ω_h) as the transfer rate from Infected to Recovered (resp. Recovered to Susceptible) for human beings. Given the time scale of the simulation, we took into account demography only for the vector: h_v was the emergence rate given a population and the time t and μ_v was the vector mortality rate.

Trade exchanges between countries were represented by a *proxy*: the traffic of trucks carrying goods between the cities present along the EWEC corridor. The trade exchange model required these three steps at three different time scales:

- (Each year) Update of country economic growth and export value.
- (Each day) Truck creation: each country, based on its export value, created a number of trucks in their cities and provided them with targets in other countries.
- (Each simulation step) Truck movement: trucks moved back and forth from their origin to their target (and conversely) and were removed when they came back.

This model was coupled with the previous one by a very simple control function: at each simulation step, trucks moving along the roads had a probability to deposit, on the corresponding cell, infected mosquitoes and/or people. This probability depended on the infection rate at their city of origin: the higher the infection was, the higher the probability that a truck could “carry” infected mosquitoes.

RESULTS

The outcome of the simulations conducted for the years 2004-2012, presented in Philippon *et al.*, 2016 showed the clear impact of the corridor development on the increase in dengue cases and on the distribution of their spatial patterns, both appearing to be strongly correlated to the data collected in the corresponding provinces.

However, the interest in integrated models like this one goes beyond uncovering causal relationships, as they can also serve prospective purposes. We demonstrated this by exploring its dynamics in a number of climatic and economic scenarios and finally used it in a participatory setup (Guyot *et al.*, 2005) to understand the importance of coordinating the control policies of the four countries involved. These two developments have allowed us to highlight the central role that models play in supporting the decision of policy makers and to plead for a more widespread use of simulations in the design of public health policies.

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