

Mathematical Approaches to Infectious Disease Prediction and Control

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SHORT COMMUNICATION

Mathematical modeling involves using mathematics to describe, explain or predict behavior or phenomena in the real world. This modeling can be particularly useful for deepening questions or testing ideas in complex systems. A mathematical model is an abstraction of a physical system using precise language to describe the behavior of the system. The model is then analyzed, solved or simulated on a computer. The results can be interpreted in physical terms to help understand the underlying system or to identify parts of the system that may be subject to change.

Mathematical modeling is born thanks to malaria. This scientific methodology, which describes the spread of disease through mathematical equations, has been and is increasingly being used to design effective public health strategies. A bacteriologist in the British Army and a recognized entomologist, Ronald Ross is certainly the Hall of Fame of scientists who have worked on malaria. It was at the end of the 19th century that he observed the presence of plasmodium in mosquito stomachs of the genus *Anopheles*, thus confirming their involvement in the transmission of malaria. This discovery, crowned by the Nobel Prize for Medicine in 1902, then allowed to lay new foundations for scientific research on this disease as well as to consider its control. It was then that he understood, before any scientific community, the importance of modeling in the transmission of this disease in order to understand how to fight it most effectively. It was in 1911, when mathematical epidemiology was virtually non-existent at the time, that Ross published the first mathematical model on malaria. It will take 15 years for Kermack and McKendrick to make new developments on this model and another 15 years for this model to re-emerge and begin to be really studied in depth.

These last decades have been marked by the emergence of numerous human and animal infectious diseases, with an important impact on public and veterinary health (Amaral & Ottino, 2004; Jones et al., 2008; Hou & Teng, 2009). The majority of the pathogens responsible for these emergences are of zoonotic origin (> 60%), and among these, more than 70% have as reservoir an animal species belonging to the wild fauna (Jones et al., 2008). On the other hand, the share of vector-borne diseases among emerging diseases has increased significantly. Different types of factors are implicated in these recent emergences, be they genetic, biological, but also environmental, climatic, or political, economic, demographic and societal (Lanska, 1998; Patz et al., 2004). In this context, many research works have developed an ecosystem approach to vector and zoonotic infectious diseases, or health ecology approach. Vector-borne diseases and malaria in particular have a strong link with the environment. The latter has indeed an influence on the host populations, vectors, pathogens and their interdependencies. More specifically, relations between environment and vectors are particularly complex: the conditions environmental factors will influence vector populations by providing them with biotopes and habitats favorable or not, and interfering with their development cycle.

A model is a simplified representation of a real system that aims, in the case of vector-borne diseases, to improve the understanding of transmission mechanisms, to represent or to predict them (Meyers, 2007). Two broad categories of models can be distinguished including conceptual models that qualitatively describe the interactions of the studied system and mathematical models that quantify the relationships or interactions in the system under study. These two categories should not be opposed since, ideally, they intervene successively in the modeling process. Within mathematical models, empirical

(or statistical) and theoretical models can be distinguished. Empirical models are data-driven and aim to investigate the statistical relationships between the variables studied, and are used to increase knowledge of the epidemiology of the disease. Theoretical models aim at them, based on important preliminary knowledge and strong hypotheses of cause-effect relationships, to simulate the epidemiology of the disease in a given context and to study the variations of its parameters.

The modeling of the dynamics of infectious diseases in the human and animal population does not date from today (Bernoulli, 1760; Hamer, 1996). Then, many biomathematical work will further theorize the transmission of infectious agents (Kermack et al., 1932). On the basis of these pioneering works and those that followed, public health research has developed on known or emerging infectious risks, which makes it possible, through the rational use of models, to propose predictions under uncertainty and evaluate the impact of different management options on the agent's transmission and thus on the resulting epidemic. This last aspect gives a strong finalized value to the modeling of infectious diseases hence its growing importance in decision support. In the history of infectious disease modeling, the pioneering work of Ross (1911) and Mac Donald (1957) on malaria transmission is a reference and has introduced the fundamentals of vector-borne infectious risk modeling. Developed from an action perspective, the model of Ross and Mac Donald has defined the fundamentals of the fight against vector-borne infections including vector control measurements. Syndromic surveillance is defined as an investigative approach in which health authorities, assisted by an automated data transmission system, are able to monitor disease indicators in real time in order to detect early emergence (Meyers et al., 2005). Interest in these means of surveillance has developed since September 11, 2001, first of all for the detection of bioterrorist attacks, and then their use has been extended to the surveillance of infectious diseases (Relay et al., 2003). Its objective is to identify aggregates of patients even before having a confirmation of the diagnosis by the laboratory, in order to implement measures of control and prevention (Buehler, 2004). To validate the results, sensitivity, defined as the proportion of weeks with alert actually followed by an epidemic and specificity, defined as the proportion of weeks without alert not followed by epidemics must be assessed. Other parameters then make it possible to

determine the usefulness of these systems including early warning and the possibility of implementing control measures, acceptability, stability and cost-effectiveness.

Let us consider the simple case of a horizontally transmitted parasite (i.e. as opposed to the vertical transmission that takes place between parents and offspring) and directly (i.e. by direct contact between individuals, without the intervention of a vector). To describe the dynamics of the epidemic, healthy, potentially infective hosts and infected hosts that can transmit the disease are identified in the population. Infection takes place if an infected individual meets a healthy individual and if the parasite is transmitted at this meeting; infected individuals can die from infection, or heal and become healthy (and re-infectable). To this epidemiological dynamic is added a demographic dynamic: new healthy individuals enter the system by birth or migration from other populations; individuals can also disappear naturally.

Mathematical models prove to be of great help and we leave a rigorous experimental system (Jones et al., 2008; Hou & Teng, 2009). In all these situations, frequent in science, the mathematical models allow us to fill the gaps of observations and to tend towards an overall comprehension of the problem, in spite of partial data. Just as a paleontologist reconstructs a dinosaur skeleton from bone fragments, an archaeologist restores a Roman mosaic or a Greek statue from a few partial elements, the biologist can hope to tend towards a global understanding of a system from which it can measure only a few variables. The data is the tip of the iceberg. Mathematical models allow us to extract the maximum amount of information from the data available to access the immersed part of the iceberg, which is not directly observable. Depending on the situation, the emergee part of the iceberg is more or less important. It is maximum in the ideal experimental devices. In such situations, statistical models make it possible to answer the question posed directly. Statistical models estimate simple relationships between different observed variables and test the significance of these relationships. The strong point of the statistical models is related to their inference power conferred by hypothesis tests. These tests of hypotheses are effective as one is in a very rigorous framework. The weak point of the statistical models is related to this framework which imposes relations between extremely simple variables (often linear). These

relationships are essentially descriptive and in no way allow access to an understanding.

In order to improve the control of vector-borne diseases in particular and to better anticipate and prevent their risk of emergence, modeling is a tool that can be used to better understand the epidemiological cycle of transmission which depends on the characteristics of all the actors involved and their interactions and to develop the tools operational data allowing the prediction of zones and periods at risk or their simulation according to different scenarios. Different types of models have been developed for vector-borne diseases including geographical models which can be used to describe the distribution of vectors according to environmental conditions (Shekhar et al., 2002), and epidemiological models related to the calculation of vector capacity and baseline reproductive rate of the disease (Hay et al., 2008).

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