



Marius Gilbert graduated in Agricultural and Applied Biological Sciences at the “Université Libre de Bruxelles” (ULB, Brussels, Belgium) in 1995. He was a visiting researcher for two years at the department of Zoology, University of Oxford, and finished his PhD on the spatial ecology of the bark beetle *Dendroctonus micans* at the ULB in 2001. He was then a post-doctoral fellow at the “Fonds National de la Recherche Scientifique” (FNRS, Brussels, Belgium) for three years, followed by three years of research at the ULB on contract research. In 2006, he was awarded a “Research Associate” permanent academic position with the Belgian FNRS, hosted at the ULB. His research deals with the spatial epidemiology of harmful organisms, insects and animal diseases, using a range of spatial modeling and spatial statistic tools.

His work initially focused on the spatial ecology of invasive insects. In the last 10 years, he became interested in the way concepts and methods usually applied to invasion ecology could be used to improve our understanding and modeling of epidemiological study systems, and started working on several animal diseases such as Bovine Tuberculosis (BTB), Foot and Mouth Disease (FMD), and Highly Pathogenic Avian Influenza (HPAI). Much of Marius Gilbert’s research over the last few years has focused on HPAI H5N1 in Asia, in close cooperation with the Food and Agriculture Organization (FAO) Animal Health division (J. Slingenbergh, T. Robinson, S. Newman, V. Martin) and those lead to key publications on the spatial epidemiology of the disease across Asia. Other key collaborators are from the University of Oklahoma (Prof. X. Xiao), from the Royal Veterinary College (D. Pfeiffer), CIRAD (F. Roger, J. Cappelle), and the Department of Zoology in Oxford (W. Wint, S. Hay).

## **MARIUS GILBERT**

*Universite Libre de  
Bruxelles  
Belgium*

He is now particularly interested in trying to better understand how changes in agricultural production, in particular intensification of animal production systems, influence the emergence and spread of animal diseases with zoonotic potential.

# SPATIAL EPIDEMIOLOGY OF HIGHLY PATHOGENIC AVIAN INFLUENZA H5N1 IN POULTRY:

What have we learned? What can be improved ?

**GILBERT M<sup>1,2\*</sup>, ROBINSON T<sup>3</sup>, NEWMAN S<sup>3</sup>, MARTIN V<sup>2</sup>, VAN BOECKEL T<sup>1,2</sup>  
HOGERWERF L<sup>1</sup>, SLINGENBERGH J<sup>3</sup>, XIAO X<sup>4</sup>**

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Highly pathogenic avian influenza (HPAI) H5N1 has spread to more than 60 countries, covering a variety of agro-ecological, economic and environmental conditions. Whilst the disease has been eradicated from most regions to which it was introduced, it persists in others, where it continues to affect the livelihoods of smallholders, to constrain development of the poultry sector, and to cause occasional human fatalities. For several years, the spatio-temporal patterns of HPAI H5N1 outbreaks (or indicators of virus presence such as positive identification) has been studied with two main aims. First, to identify risk factors associating with the presence of the virus such as to guide intervention and changes in prevention measures and policies. Second, to map the geographical distribution of the risk of HPAI H5N1 virus presence, so that surveillance and control could be better targeted.

## ***OF DUCKS, RICE... AND TRUCKS***

Some of the first publications on the distribution of HPAI H5N1 risk were produced about the situation

in Thailand (Gilbert et al. 2006) and Vietnam (Pfeiffer et al. 2007) because those countries experienced strong epidemics and quickly established efficient disease surveillance systems allowing those analyses to be done. The analyses identified the density of domestic duck as key risk factors associating with the presence of HPAI H5N1, and this supported the results of previous laboratory work highlighting that domestic duck could make asymptomatic infections (Hulse-Post et al. 2005) and spread the virus silently. Follow-up work showed that domestic duck husbandry was closely associated with intensively cropped rice (Gilbert et al. 2007), and that the remote sensing of those areas with double or triple annual production of rice could be carried out using satellite imagery, and that these data could help better mapping the distribution of HPAI H5N1 risk in the Mekong region (Gilbert et al. 2008 p. 1).

However, follow-up studies carried out in other countries such as Indonesia (Loth et al. 2011), Bangladesh (Loth et al. 2010; Ahmed et al. 2012) and South Asia (Gilbert et al. 2010) showed a

<sup>1</sup> Biological Control and Spatial Ecology, Université Libre de Bruxelles CP160/12, 50 Av. F.D. Roosevelt, B-1050, Brussels, Belgium.

<sup>2</sup> Fonds National de la Recherche Scientifique, 5 rue d'Egmont, B-1000, Brussels, Belgium.

<sup>3</sup> Food and Agriculture Organization of the United Nations (FAO), Viale delle Terme di Caracalla 00153, Rome, Italy.

<sup>4</sup> Center for Spatial Analysis, College of Atmospheric and Geographic Sciences, University of Oklahoma.

\*Corresponding author: Gilbert Marius, Tel: +32 2 650 37 80 Email: mgilbert@ulb.ac.be

different pattern, with domestic duck density not showing up as a significant risk factor, whilst other factors were found comparatively more important. A plausible explanation, already suggested in Gilbert et al. (2010) was that the difference was caused by differences in duck production systems. This hypothesis was tested by going back to the Thailand data set, separating chicken and duck data extensive and intensive production systems (Van Boeckel et al. 2012b), and testing those new variable against HPAI H5N1 risk in Thailand. In Thailand, it was found that the variable most strongly associated with HPAI H5N1 risk was the duck raised intensively, with large flock having a median of approximately 5000 birds per owner (Van Boeckel et al. 2012a). Those used to be transported by truck over long distance throughout the country to be fed in rice paddy fields (Songserm et al. 2006) at the time of the epidemic, before new policy banned those long-distance movement in the absence of a negative test. In contrast, ducks raised extensively by smallholders with a flock size of 10 birds per owner were not showing a strong association with HPAI H5N1 risk, a situation that resembles that observed in Bangladesh, India and Indonesia where duck farming is largely dominated by backyard production. In China, where duck production was drastically intensified over the last few decades (Fig. 1), and where HPAI H5N1 emerged (Li et al. 2004), a recent study by Martin et al. (2011) showed that factors relating to HPAI H5N1 presence detected through active surveillance in markets also correlated with domestic waterfowls density and typical habitat.

### **OTHER FACTORS**

Many other authors have since analyzed risk factors associating with the presence of HPAI H5N1 virus, and those we recently reviewed in Gilbert & Pfeiffer

(2012). The review aimed to identify common risk factors amongst spatial modelling studies conducted in different agro-ecological systems, and to identify gaps in our understanding of the disease's spatial epidemiology. Three types of variables with similar statistical association with HPAI H5N1 presence across studies and regions were identified: domestic waterfowl, several anthropogenic variables (human population density, distance to roads) and indicators of water presence. Variables on socio-economic conditions, poultry trade, wild bird distribution and movements were comparatively rarely considered. Surprisingly, the density of chicken did not show a consistent association with HPAI H5N1 risk across studies and scales. This variable may cover a diversity of types of farming with extremely variable levels of bio-security, hygiene and disease prevention practices. Differences of the type of chickens (native vs. improved breeds), how they are raised (backyard vs. commercial), and how these differences were, or were not, accounted for in the studies considered in the review likely explains the differences obtained across studies. Here again, better accounting for the difference in production system may shed some light on this effect.

Three types of factors have been poorly addressed in the reviewed studies, especially if one considers their potential impact on disease transmission: i) socio-economic factors, ii) poultry trade factors, and iii) factors related to wild bird distribution. The common feature of all three factors is that there are technical difficulties in data collection. Socio-economic data (e.g. purchasing power per capita, land value, price indices) are often aggregated at a relatively coarse level, and can hence not be easily integrated into spatial modeling.

Similarly, poultry trade variables are notoriously difficult to obtain. When available, these data ignore illegal trade, which can be very significant within and between countries, and that can be further exacerbated under HPAI H5N1 epidemic conditions. Furthermore, trade patterns are extremely dynamic and can change according to production / demand discrepancies and price differences between geographic regions. A trade flow observed in a year between two regions could stop, or even reverse the following year as a result of changes in price differences between the regions. Difficulty in obtaining pertinent spatial data is also one of the main reasons explaining why so few studies have formally integrated information on wild birds in HPAI H5N1 spatial modeling. In the wild avifauna, migratory water birds of the Anatidae family are those thought to have been implicated in long-distance transmission of HPAI H5N1. However, this family includes a large number of migratory species that have an inherently dynamic distribution. Data on their distribution in space and time are hence difficult to obtain at high resolution. Furthermore, although some sites are known to harbour large wintering populations, the precise locations where birds will actually stay may vary from year to year, depending on the specifics of the water level and food availability. One can then only predict areas where the birds are likely to be, rather than where they actually are. Massive efforts have been directed toward better characterization of waterfowl migration patterns and habitat preference in the context of HPAI H5N1, and this has resulted in important advances in understanding their potential capacity to spread the virus over long distances. However, these data provide information on individuals that cannot easily be used to predict the distribution at the population level at a fine spatial scale.

## **FUTURE WORK**

Future work could improve upon previous findings in several ways.

First, we have highlighted the importance of separating poultry data into production systems, so that the respective role of smallholders, semi-intensive and industrial farming can be better disentangled. What was recently shown for Thailand is probably true also for other countries, i.e. different type of production systems are not associating with the risk equally. The current body of studies that only rarely provides adequate differentiation of poultry data into different production system categories has not provided a robust evidence base to inform the debate about their respective role in the epidemic.

Second, the same can be said about the respective role of wild birds and poultry trade in the spread of HPAI H5N1. We recognize the challenge of integrating these factors within the most commonly used modeling frameworks, and the challenge of obtaining pertinent data. However, with the emergence of the “One health” concept, that aims to more holistically integrate the key factors of the human and animal dimensions influencing emergence of infectious diseases, future work should aim at better integrating those overlooked factors into spatial models.

Third, the integration of two other dimensions of ecological system within which HPAI H5N1 occurs should also be considered in future modeling efforts: time and evolution. With few exceptions, time has been ignored in previous

studies and would deserve to be better accounted for in temporally explicit statistical modeling, where both the dependent variable and the predictors are explicit in space and time. This could help quantifying the space-time association between the distribution of water, cropping or eco-climatic variables and HPAI H5N1 risk, and help developing hypotheses on the seasonality that was observed in HPAI H5N1 epidemic curves. Along those effort, a shift from data-driven statistical modelling to more mechanistic mathematical modeling will be useful so that more explicit hypotheses can be tested. Finally, all HPAI H5N1 cases have been considered molecularly and pathogenetically identical in the spatial modeling studies, whilst the virus has evolved into a number of clades over time that could be linked to variations in pathogenicity and transmission. A better integration of phylogeographic and risk-factor type of studies, whilst methodologically challenging, would also provide much insight into the evolutionary conditions of emergence of this unprecedented panzootic.

Ahmed, S.S.U., Ersbøll, A.K., Biswas, P.K., Christensen, J.P., Hannan, A.S.M.A. & Toft, N. (2012) Ecological Determinants of Highly Pathogenic Avian Influenza (H5N1) Outbreaks in Bangladesh. *PLoS ONE*, 7, e33938.

Van Boeckel, T.P., Thanapongtharm, W., Robinson, T., Biradar, C.M., Xiao, X. & Gilbert, M. (2012a) Improving Risk Models for Avian Influenza: The Role of Intensive Poultry Farming and Flooded Land during the 2004 Thailand Epidemic. *PLoS one*, 7, e49528.

Van Boeckel, T.P., Thanapongtharm, W., Robinson, T., D'Aiotti, L. & Gilbert, M. (2012b) Predicting the distribution of intensive poultry farming in Thailand. *Agriculture, ecosystems & environment*, 149, 144–153.

Gilbert, M., Chaitaweesub, P., Parakarnawongsa, T., Premashtira, S., Tiensin, T., Kalpravidh, W., Wagner, H. & Slingenbergh, J. (2006) Free-grazing ducks and highly pathogenic avian influenza, Thailand. *Emerging Infectious Diseases*, 12, 227–234.

Gilbert, M., Newman, S.H., Takekawa, J.Y., Loth, L., Biradar, C., Prosser, D.J., Balachandran, S., Subba Rao, M.V., Mundkur, T., Yan, B., Xing, Z., Hou, Y., Batbayar, N., Natsagdorj, T., Hogerwerf, L., Slingenbergh, J. & Xiao, X. (2010) Flying over an infected landscape: distribution of highly pathogenic avian influenza H5N1 risk in South Asia and satellite tracking of wild waterfowl. *EcoHealth*, 7, 448–458.

Gilbert, M. & Pfeiffer, D.U. (2012) Risk factor modelling of the spatio-temporal patterns of highly pathogenic avian influenza (HPAIV) H5N1: a

review. *Spatial and spatio-temporal epidemiology*, 3, 173–183.

Gilbert, M., Xiao, X.M., Chaitaweesub, P., Kalpravidh, W., Premashtira, S., Boles, S. & Slingenbergh, J. (2007) Avian influenza, domestic ducks and rice agriculture in Thailand. *Agriculture Ecosystems & Environment*, 119, 409–415.

Gilbert, M., Xiao, X., Pfeiffer, D.U., Epprecht, M., Boles, S., Czarnecki, C., Chaitaweesub, P., Kalpravidh, W., Minh, P.Q., Otte, M.J., Martin, V. & Slingenbergh, J. (2008) Mapping H5N1 highly pathogenic avian influenza risk in Southeast Asia. *Proceedings of the National Academy of Sciences*, 105, 4769–4774.

Hulse-Post, D.J., Sturm-Ramirez, K.M., Humberd, J., Seiler, P., Govorkova, E.A., Krauss, S., Scholtissek, C., Puthavathana, P., Buranathai, C., Nguyen, T.D. & others. (2005) Role of domestic ducks in the propagation and biological evolution of highly pathogenic H5N1 influenza viruses in Asia. *Proceedings of the National Academy of Sciences*, 102, 10682–10687.

Li, K.S., Guan, Y., Wang, J., Smith, G.J.D., Xu, K.M., Duan, L., Rahardjo, A.P., Puthavathana, P., Buranathai, C., Nguyen, T.D. & others. (2004) Genesis of a highly pathogenic and potentially pandemic H5N1 influenza virus in eastern Asia. *Nature*, 430, 209–213.

Loth, L., Gilbert, M., Osmani, M.G., Kalam, M.A. & Xiao, X. (2010) Risk Factors and Clusters of Highly Pathogenic Avian Influenza H5N1 in Bangladesh. *Preventive Veterinary Medicine*, 96, 104–113.

Loth, L., Gilbert, M., Wu, J., Czarnecki, C., Hidayat, M. & Xiao, X. (2011) Identifying risk factors of highly pathogenic avian influenza (H5N1 subtype) in Indonesia. *Preventive veterinary medicine*, 102, 50–58.

Martin, V., Pfeiffer, D.U., Zhou, X., Xiao, X., Prosser, D.J., Guo, F. & Gilbert, M. (2011) Spatial distribution and risk factors of highly pathogenic avian influenza (HPAI) H5N1 in China. *PLoS pathogens*, 7, e1001308.

Pfeiffer, D.U., Minh, P.Q., Martin, V., Epprecht, M. & Otte, M.J. (2007) An analysis of the spatial and temporal patterns of highly pathogenic avian influenza occurrence in Vietnam using national surveillance data. *Veterinary Journal*, 174, 302–309.

Songserm, T., Jam-on, R., Sae-Heng, N., Meemak, N., Hulse-Post, D.J., Sturm-Ramirez, K.M. & Webster, R.G. (2006) Domestic ducks and H5N1 influenza epidemic, Thailand. *Emerging Infectious Diseases*, 12, 575–581.

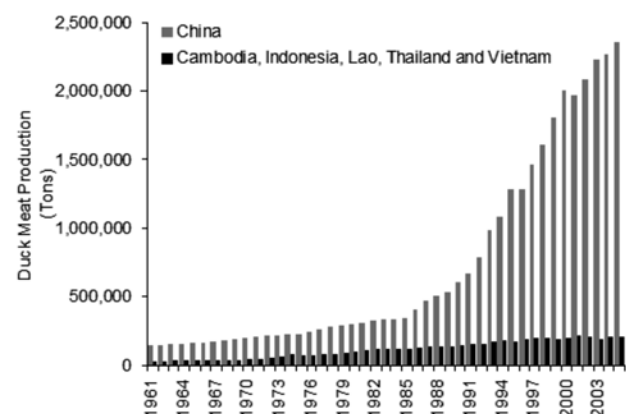


Fig. 1 Total production of duck meat in China (grey) and summed over Cambodia, Indonesia, Lao, Thailand and Vietnam between 1961 and 2006 (source: FAOSTAT 2006)