Avian, Pandemic and Seasonal Influenza

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NASA Goddard Space Flight Center

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Decision Support & Research Partners

- USDA Animal & Plant Health Inspection Service
- US Naval Medical Research Unit-2
- US DoD GEIS Central Hub
- US CDC Influenza Division
- US CDC Global Disease Detection Program
- Wetlands International Indonesia Programme
- Cobb Indonesia


H5N1 AI — THE PROBLEM

- First appeared in Hong Kong in 1996-1997, HPAI has spread to approximately 60 countries. More than 250 million poultry were lost.

- 35% of the human cases are in Indonesia. Worldwide the mortality rate is 53%, but 81% in Indonesia. In Indonesia, 80% of all fatal cases occurred in 3 adjacent provinces.

- Co-infection of human and avian influenza in humans may produce deadly strains of viruses through genetic reassortment.

- HPAI H5N1 was found in Delaware in 2004.

- The risk of an H5, H7 or H9 pandemic is not reduced or replaced by the 2009 H1N1 pandemic.

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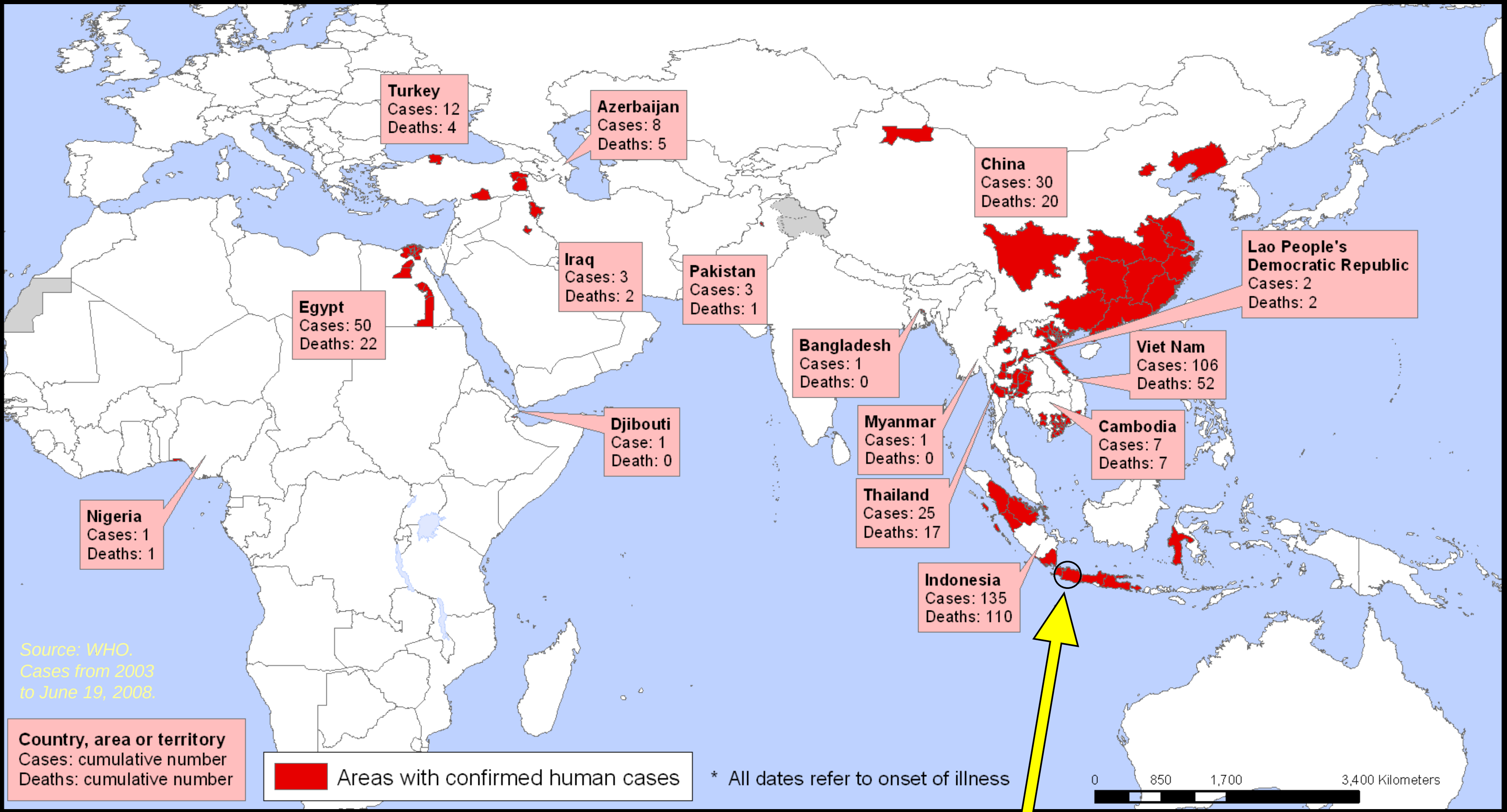
Indonesia has 35% of the world's human cases with 81% mortality. For the rest of the world, mortality is 53%.



80% of the deaths in Indonesia occurred in this region.

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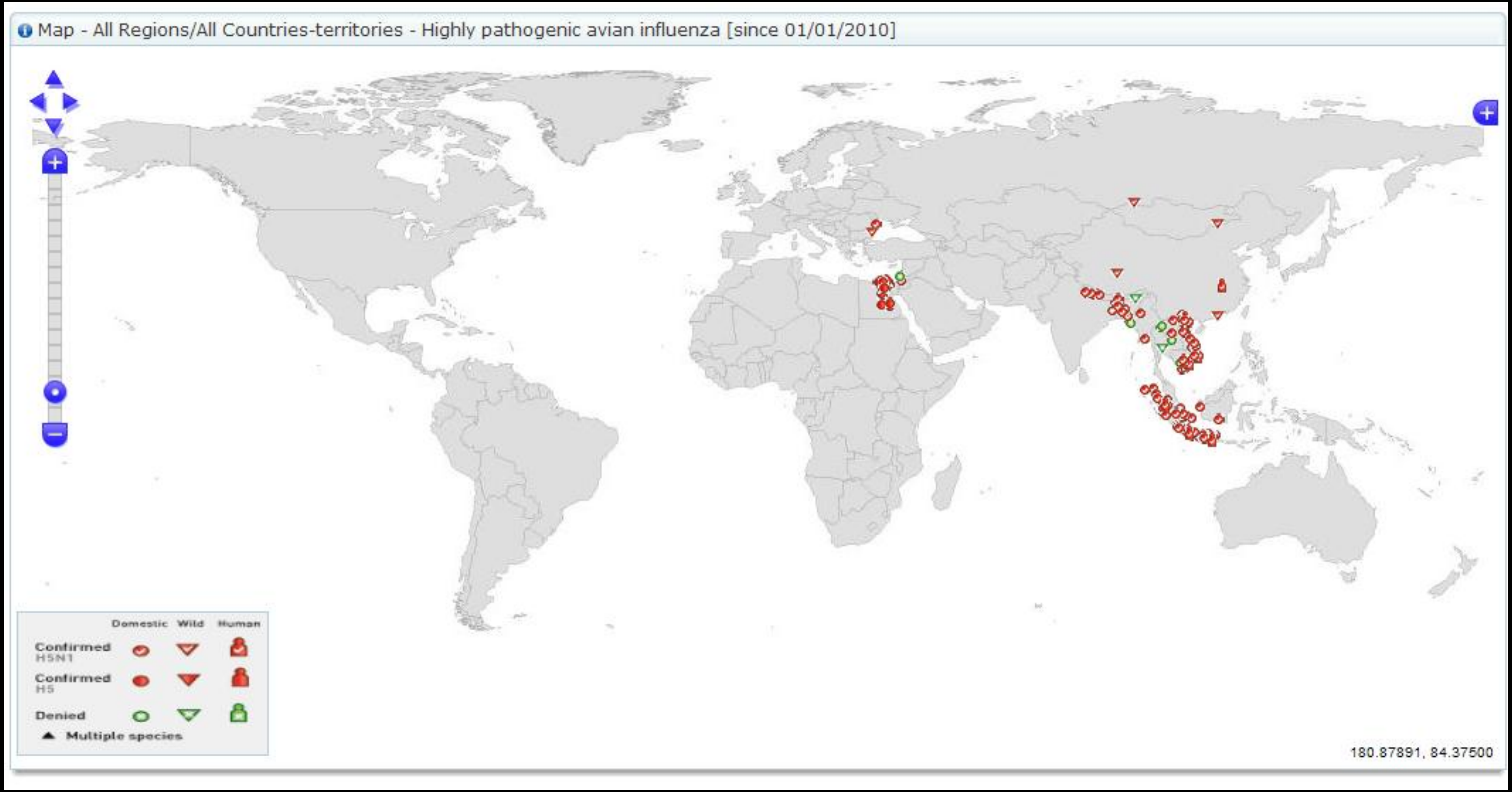
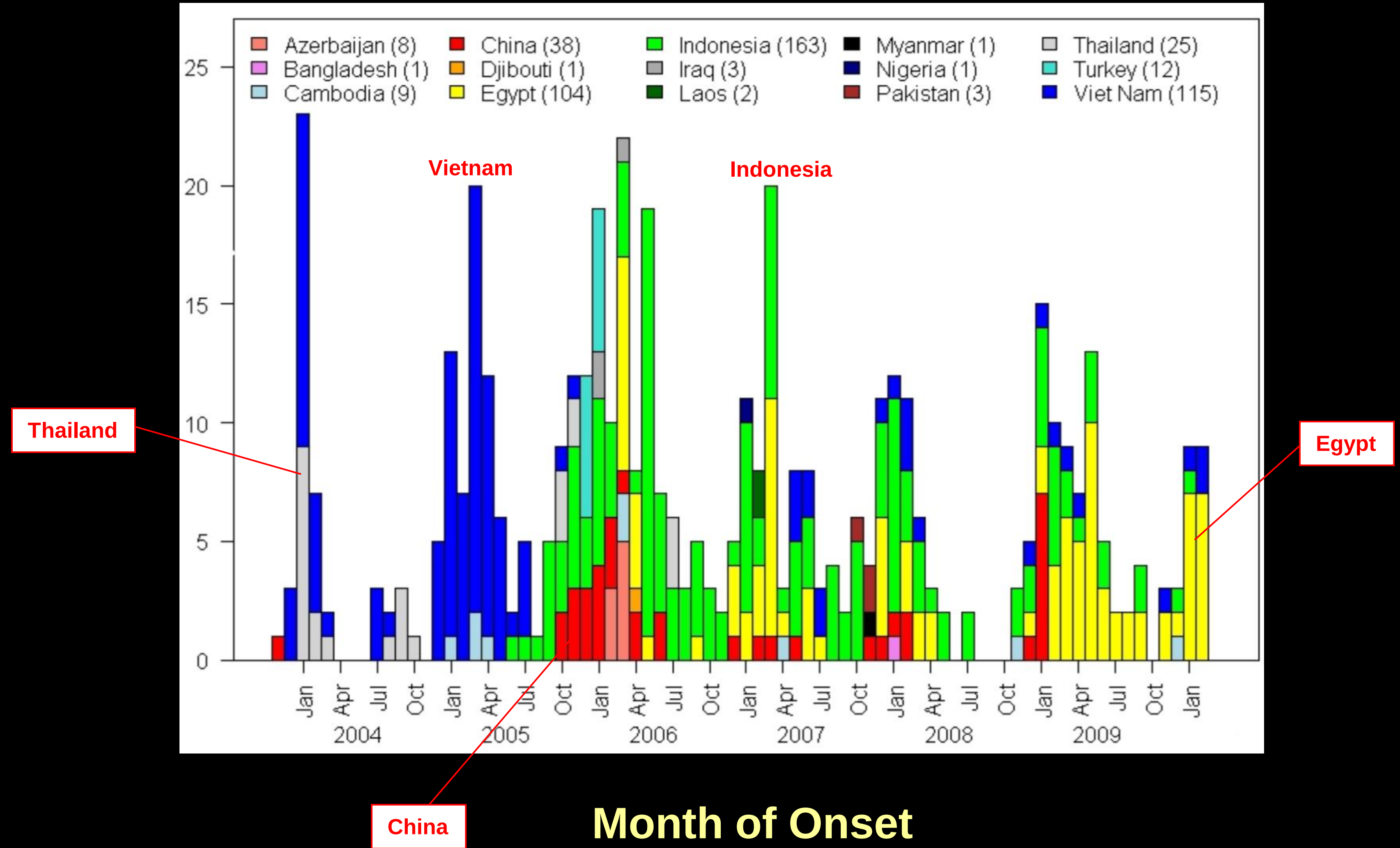
Highly Pathogenic AI Poultry Cases Since January 2010

FAO EMPRES



Confirmed H5N1 Human Cases

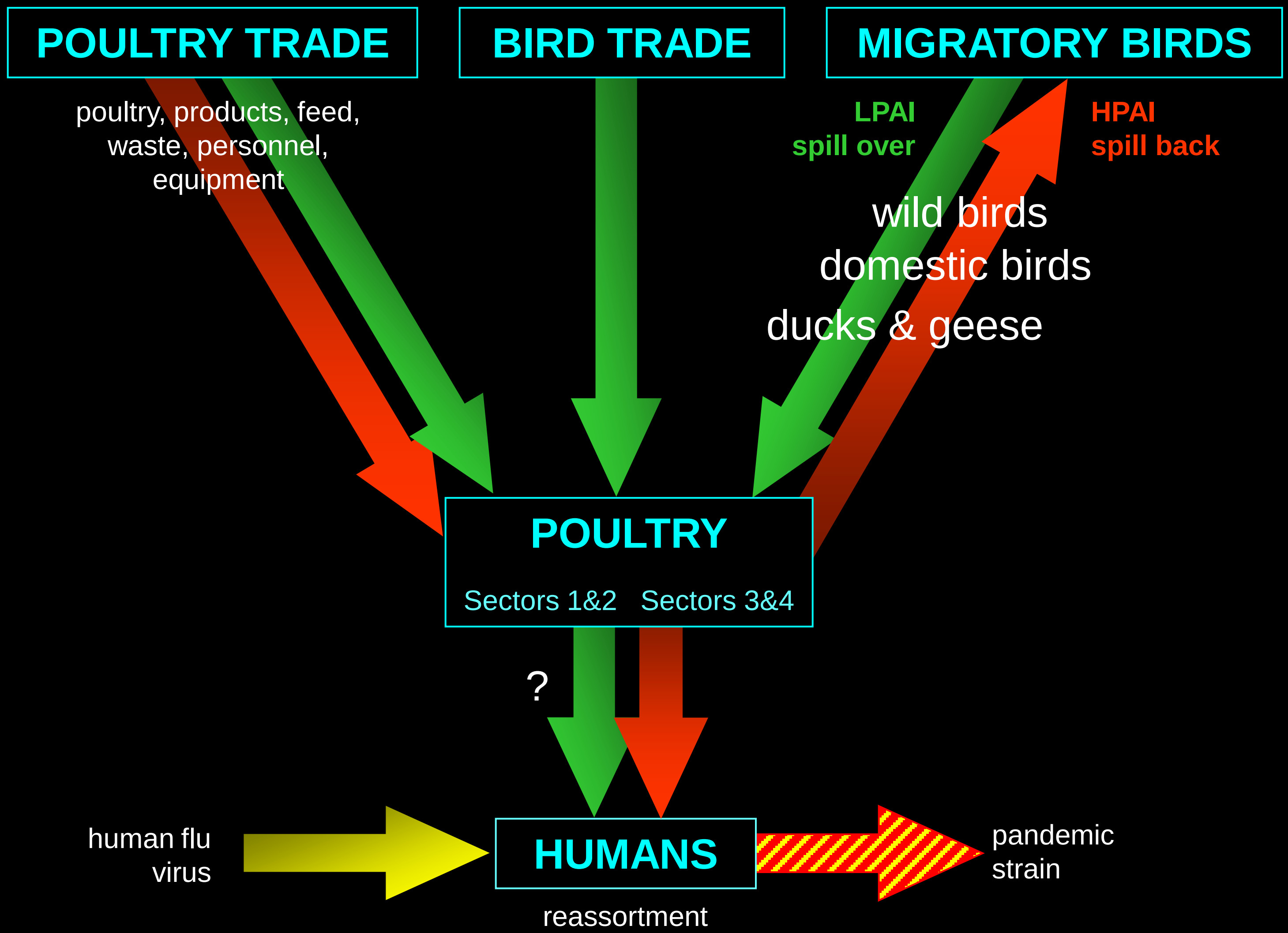
As of March 4, 2010



Month of Onset

From: F. Mahoney / CDC-Indo

H5N1 TRANSMISSION PATHWAYS



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Questions to Answer in 4 Objectives

1 What environmental and socio-economical factors may contribute to highly pathogenic AI outbreaks?

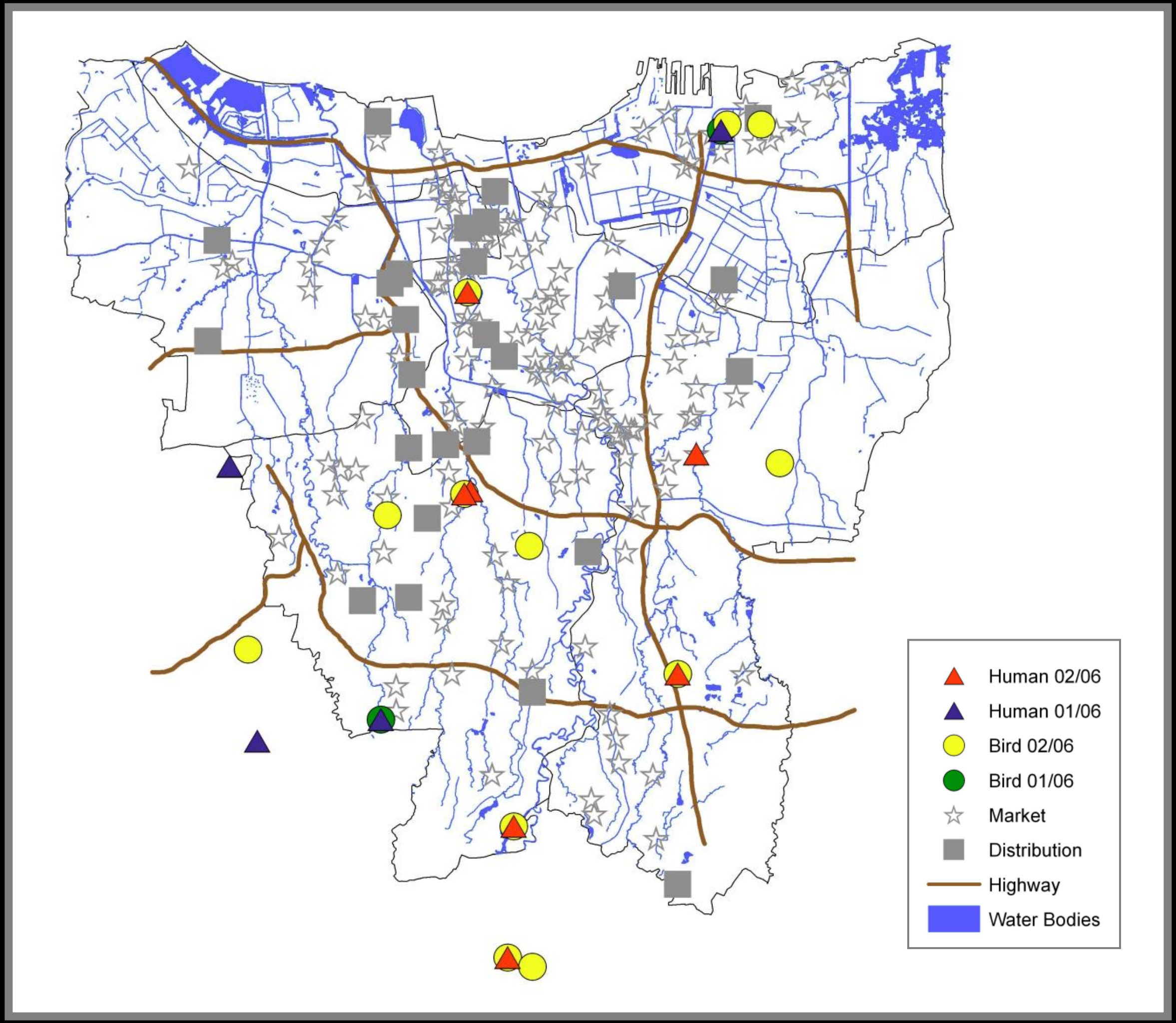
2 What areas around wetlands may have higher risks for AI outbreaks?

3 How do AI viruses spread on and off farms, within and across poultry sectors, and into the environment?

4 How is influenza transmission influenced by the environment? How can this be used for forecasting and pandemic early warning?

Poultry Outbreaks, Human Cases, Wet Markets, And Distribution Centers in Greater Jakarta

January – February 2006



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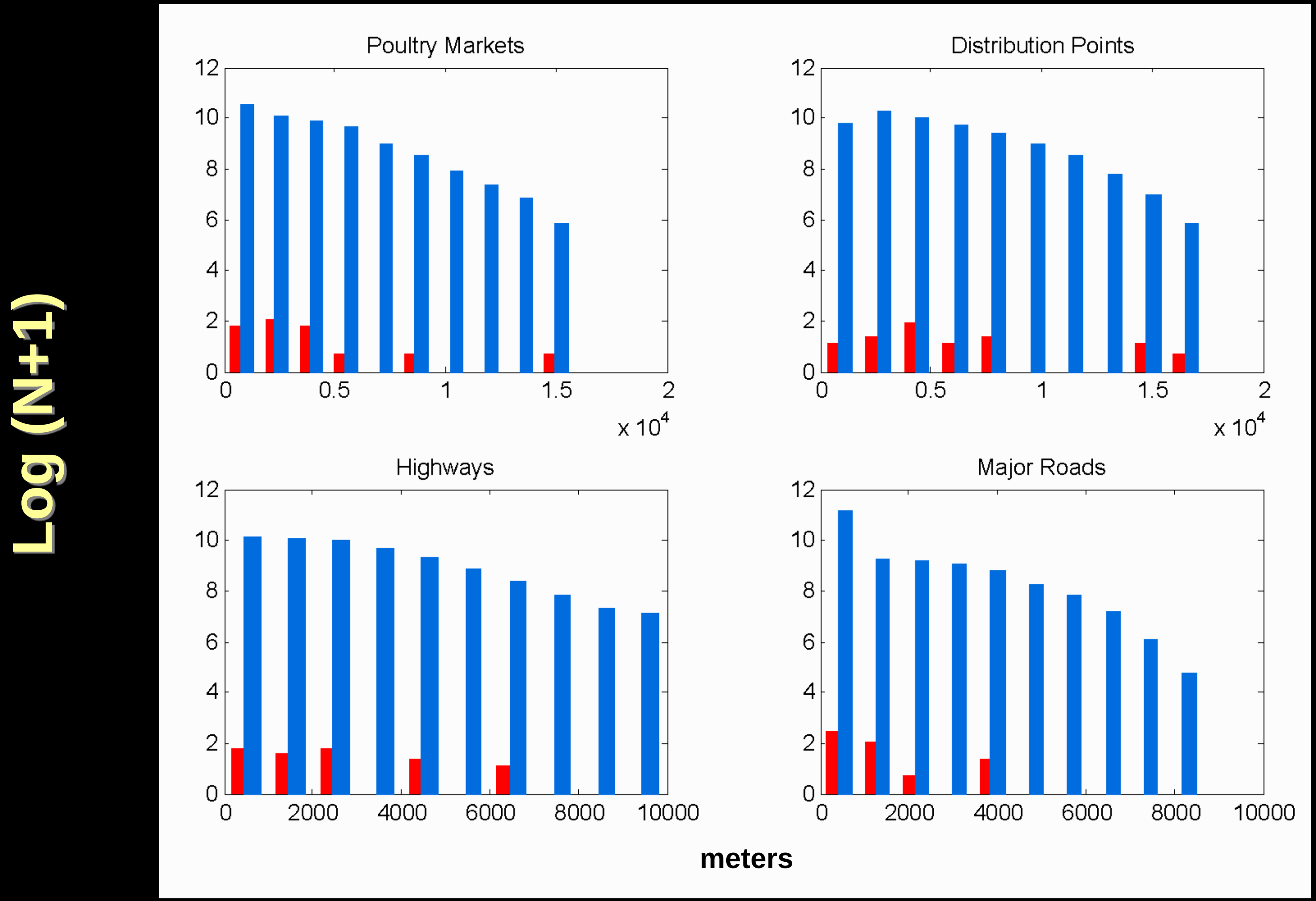
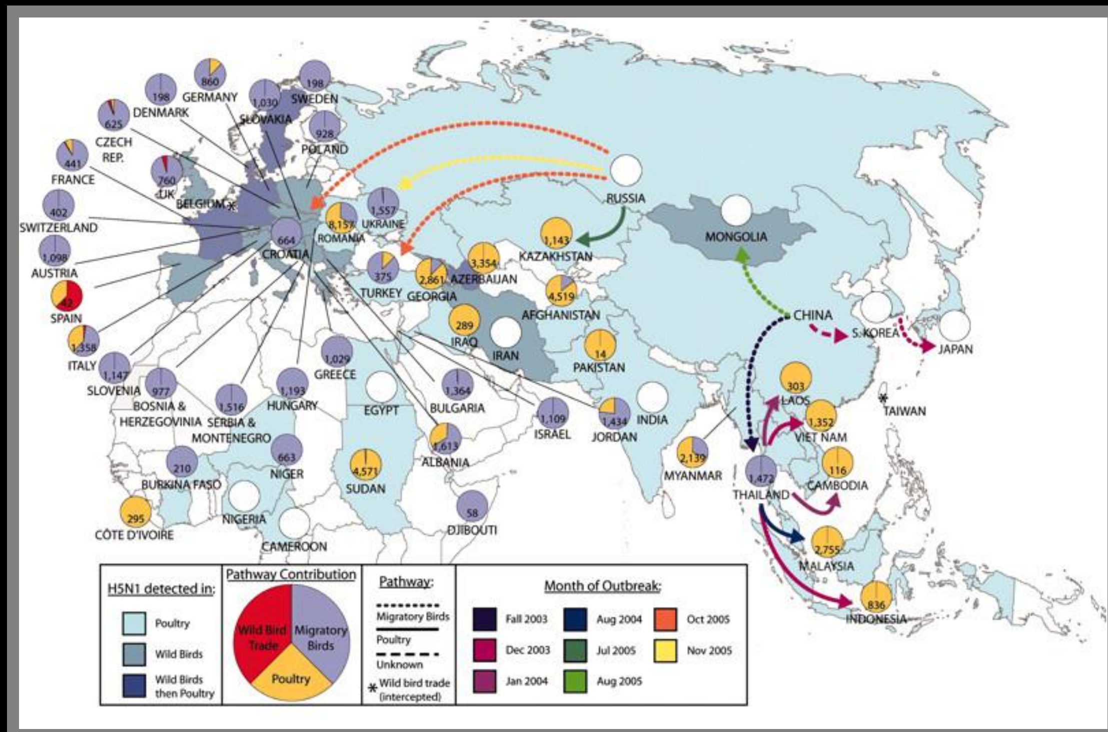
Histograms of Distance from Neighborhoods With/without Outbreaks to Other Locations



Analysis of Global Spread of H5N1 through Phylogenetic Evidence, Poultry & Bird Trades, And Bird Migration Data

Europe

87% thru mig. birds



Source: Kilpatrick et al., PNAS 2006.

US

Most likely thru poultry to surrounding countries first, then thru migratory birds to US mainland

Africa

25% thru poultry
38% thru mig. birds

Asia

43% thru poultry
14% thru mig. birds

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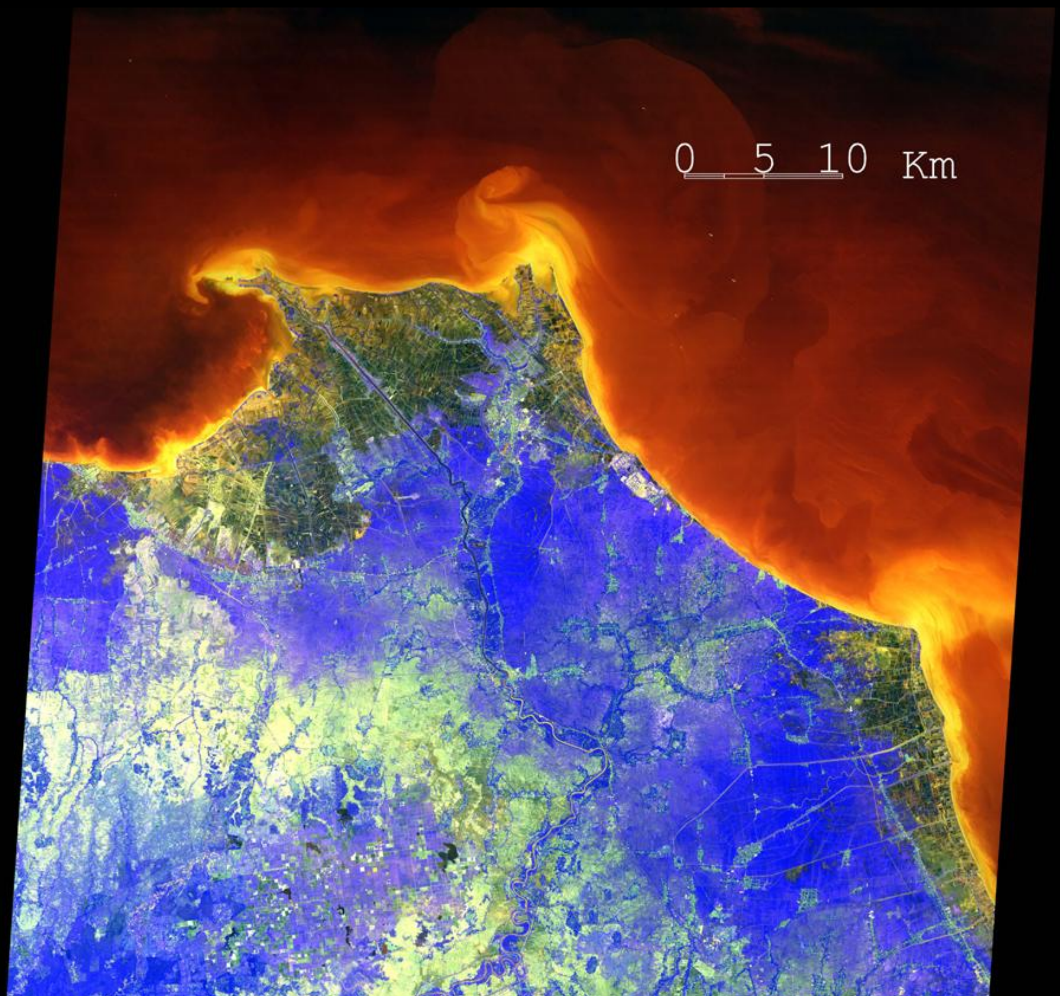
Buffer zones can be established to limit the spread of H5N1 around wetlands and the nearby farmlands



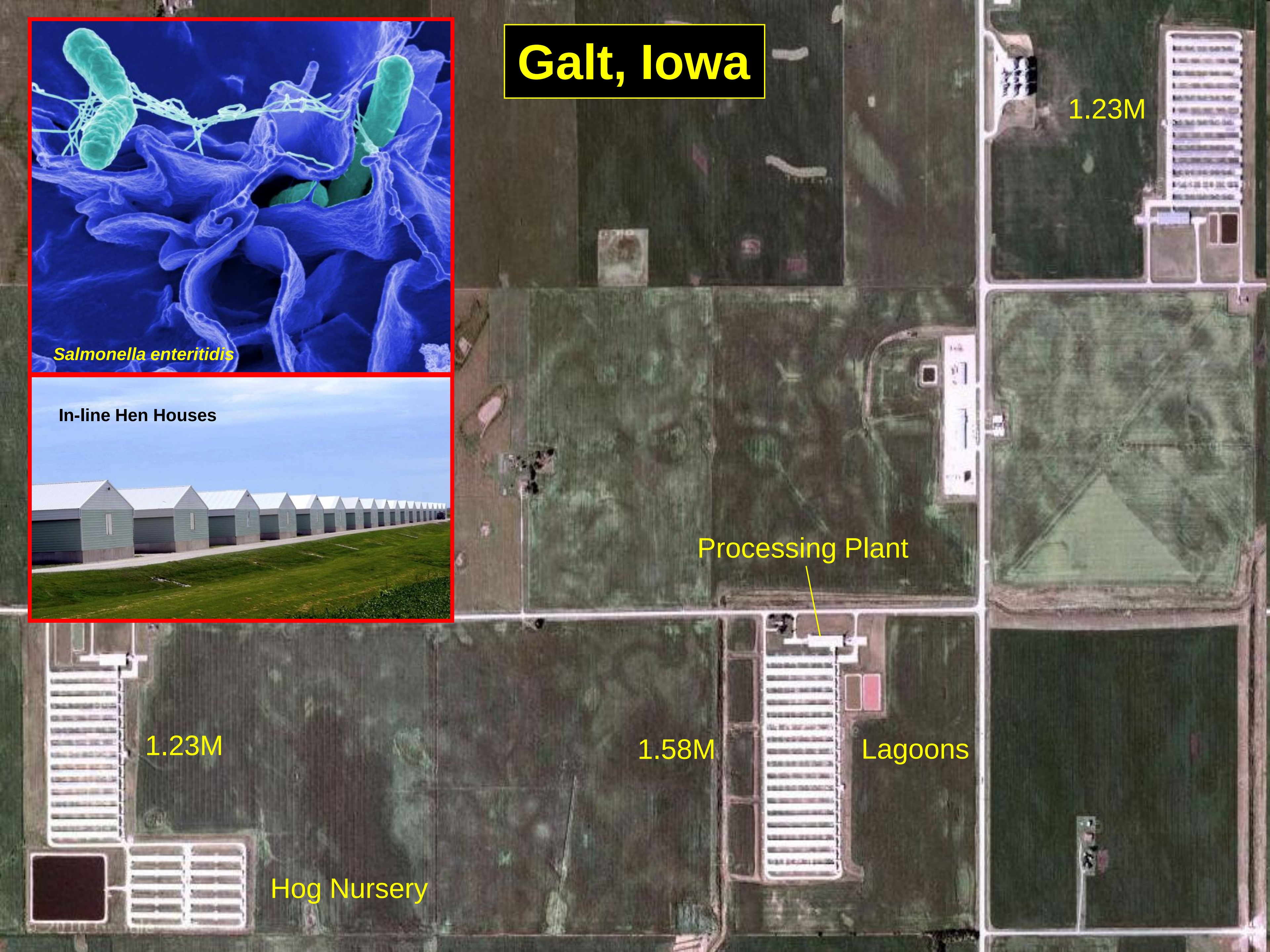
EU's & UK's Practice:

3 km protection zone
10 km surveillance zone
larger restricted zone

ASTER image showing NAMRU-2 bird surveillance site around Muara cimanuk estuar

Densely Populated Sector I Poultry Production Area Near Jakarta

Galt, Iowa


Salmonella enteritidis
In-line Hen Houses
1.23M
Processing Plant
1.23M
1.58M
Lagoons
Hog Nursery

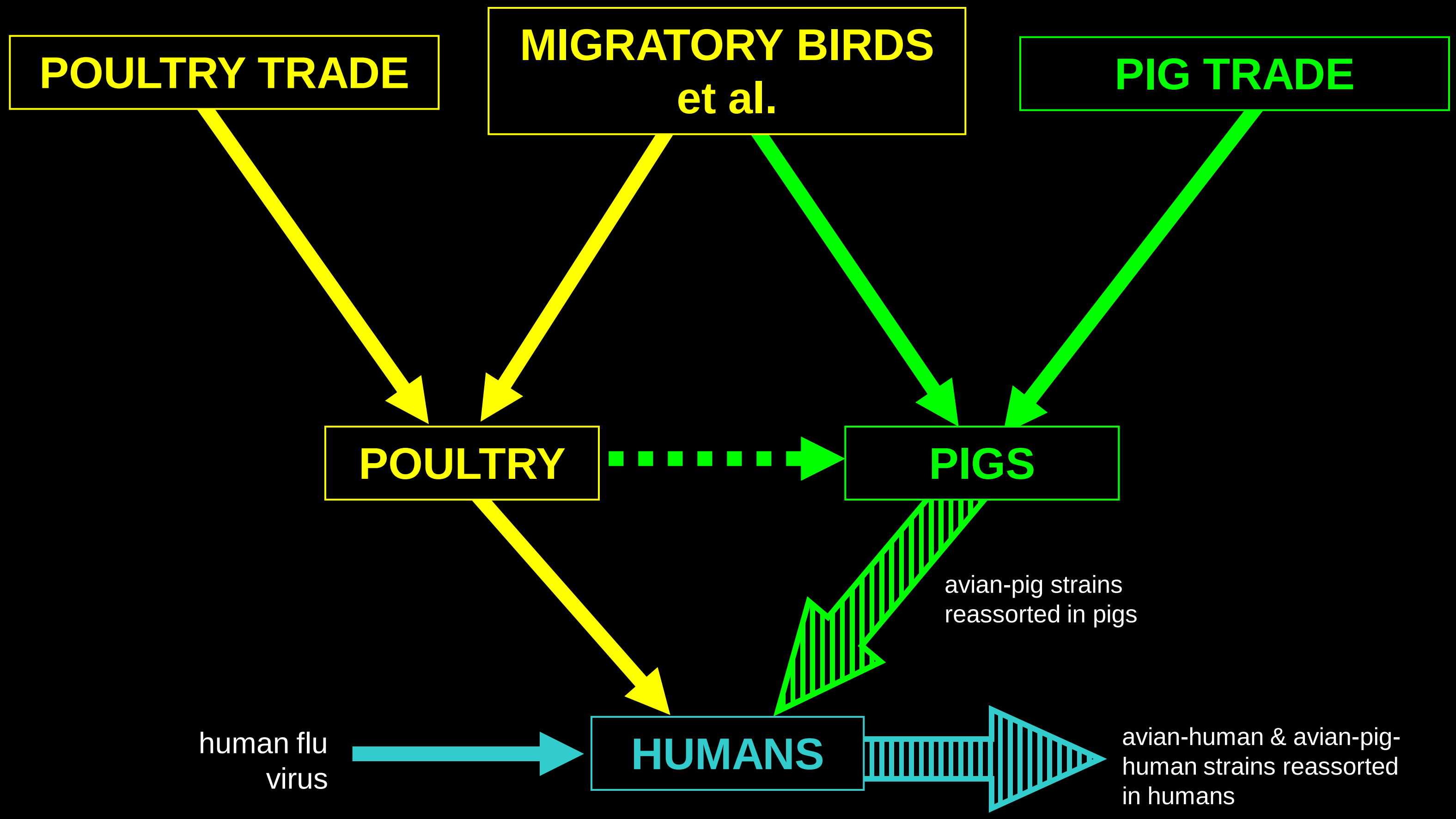
EID Vol. 16 No. 7
July 2010

Novel Swine Influenza Virus Reassortants in Pigs, China

Yuhai Bi,[1] Guanghua Fu,[1] Jing Chen,[1] Jinshan Peng, Yipeng Sun, Jingjing Wang, Juan Pu, Yi Zhang, Huijie Gao, Guangpeng Ma, Fulin Tian, Ian H. Brown, and Jinhua Liu

During swine influenza virus surveillance in pigs in China during 2006–2009, we isolated subtypes H1N1, H1N2, and H3N2 and found novel reassortment between contemporary swine and avian panzootic viruses. These reassortment events raise concern about generation of novel viruses in pigs, which could have pandemic potential.

TRANSMISSION PATHWAYS WITH PIGS INCLUDED



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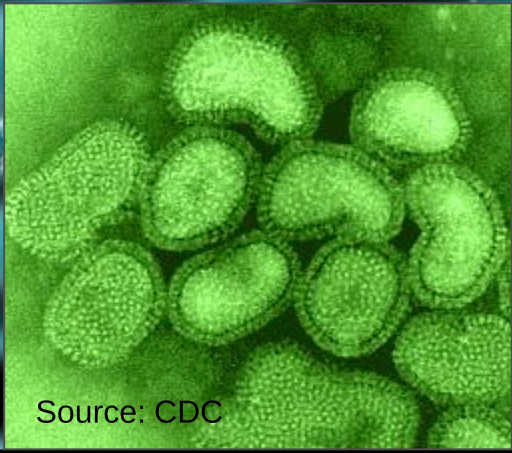
Objective 4
Modeling Seasonal Influenza

How does seasonality vary geographically? How is influenza transmission influenced by the environment? How can this be used for forecasting and pandemic early warning?

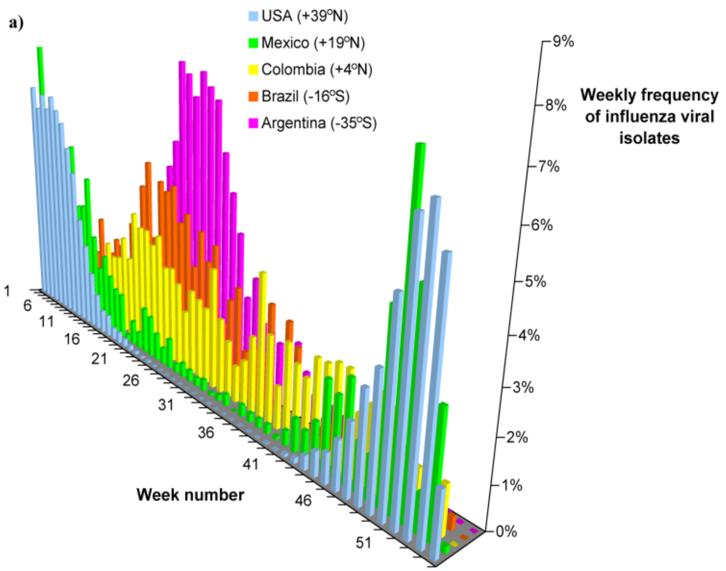
Cilia being invaded by flu virus
Source: National Geographic



Source: CDC

Influenza Burden and Seasonality

- Worldwide annual epidemics
  - Infects 5 to 15% of population, 500,000 deaths
- Economic burden in the US ~$87.1 billion [Molinari 2007]
- Spatio-temporal pattern of epidemics vary with latitude
  - role of environmental and climatic factors
- Temperate regions: distinct annual oscillation with winter peak
- Tropics: less distinct seasonality, and often peak more than once a year



Viboud et al. (2006). PLoS Med 3(4):e89

Influenza Factors

Factors that have been implicated in influenza

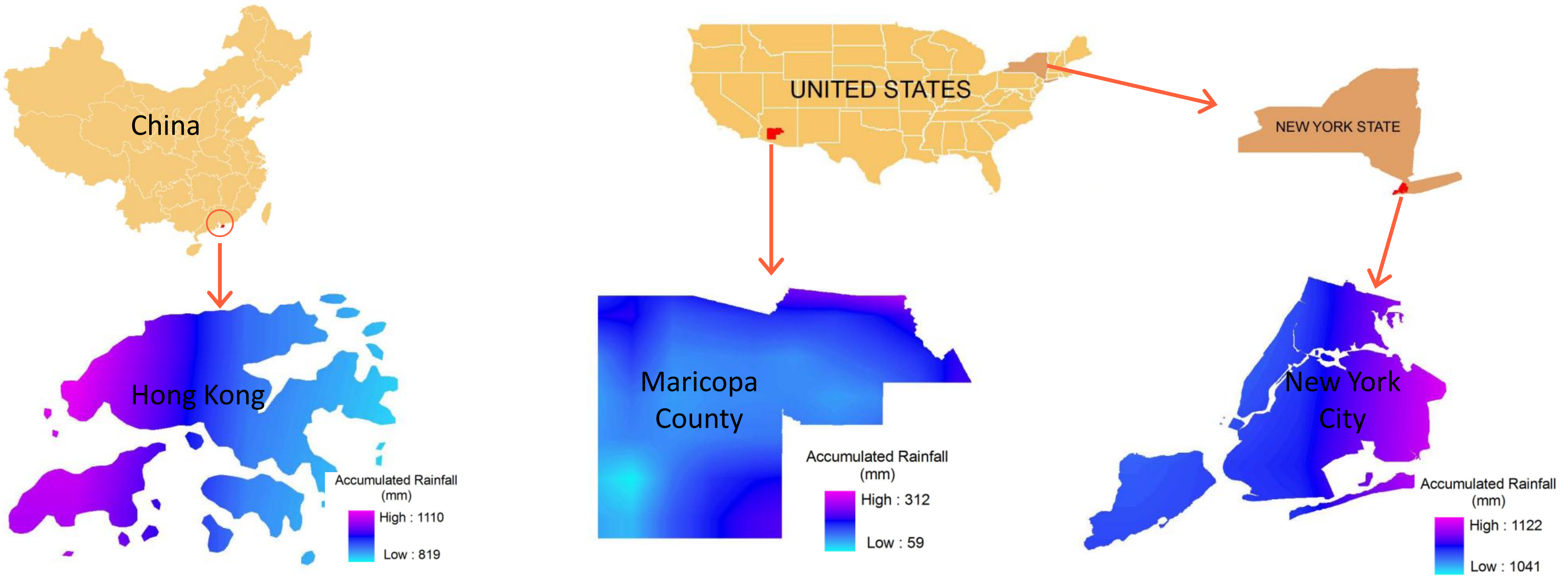
Influenza Process	Factors	Relationship
Virus Survivorship	Temperature	Inverse
	Humidity	Inverse
	Solar irradiance	Inverse
Transmission Efficiency	Temperature	Inverse
	Humidity	Inverse
	Vapor pressure	Inverse
	Rainfall	Proportional
	ENSO	Proportional
	Air travels and holidays	Proportional
Host susceptibility	Sunlight	Inverse
	Nutrition	Varies

Objective

- Systematically investigate the effect of meteorological and climatic factors on seasonal influenza transmission
- Understanding influenza seasonality provides a basis on how pandemic influenza viruses may behave
- Develop framework for influenza early warning and pandemic influenza early detection

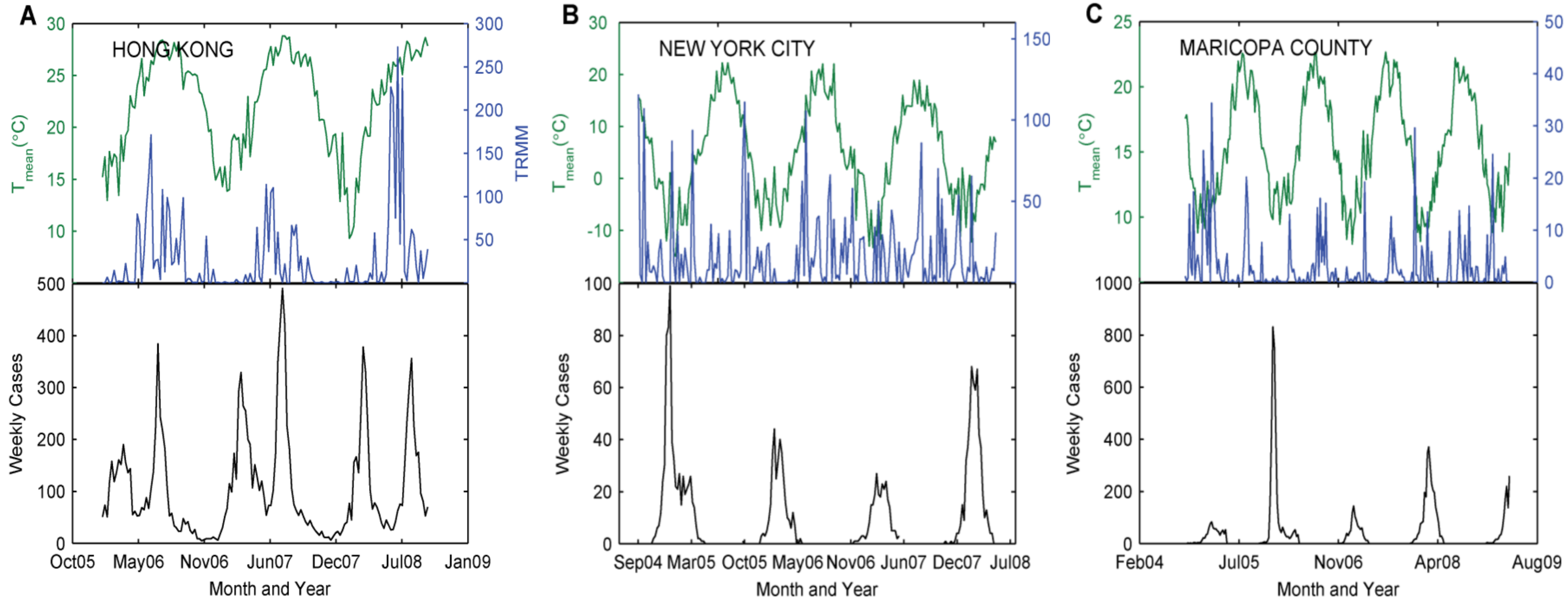
Examples

	Hong Kong, China	**Maricopa County,** Arizona	**New York City,** New York
Center Lat.	22° N	33° N	40° N
Climate	Sub-Tropical	Sub-Tropical	Temperate
General Condition	Hot & humid during summer. Mild winter, average low of 6°C	Dry condition. Mean winter low is 5°C, and summer high is 41°C	Cold winter, average low of -2°C. Mean summer high is 29°C



Data

- Weekly lab-confirmed influenza positive
- Daily environmental data were aggregated into weekly
- Satellite-derived data
  - Precipitation – TRMM 3B42
  - Land Surface Temperature (LST) – MODIS dataset
- Ground station data



Methods

- *Several techniques were employed, including:*

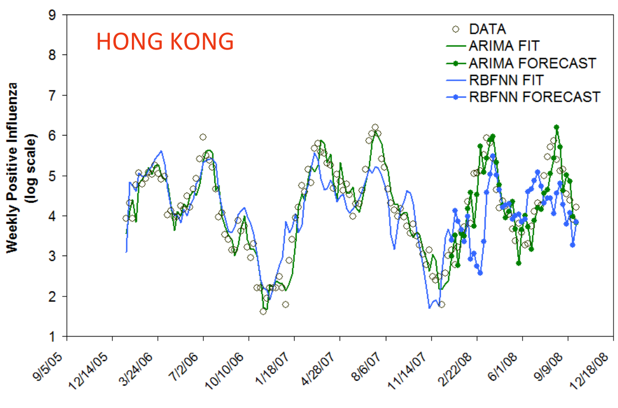
***ARIMA* (AutoRegressive Integrated Moving Average)**

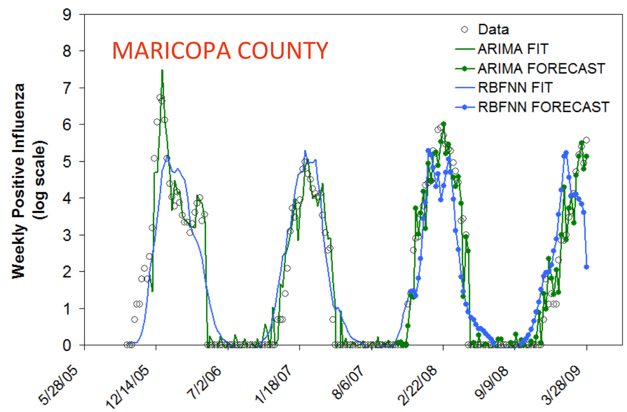
- Classical time series regression Accounts for autocorrelation and seasonality properties
- Climatic variables as covariates
- Previous week(s) count of influenza is included in the inputs
- Results published in PLoS ONE 5(3): 9450, 2010

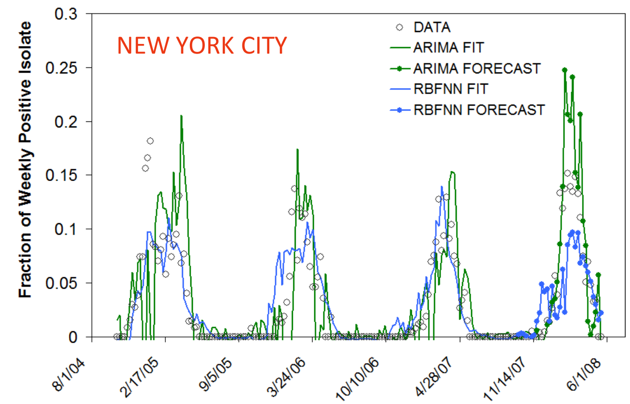
***Neural Network* (NN)**

- Artificial intelligence technique
- Widely applied for
  - approximating functions,
  - Classification, and
  - pattern recognition
- Takes into account nonlinear relationship
- Radial Basis Function NN with 3 nodes in the hidden layer
- Only climatic variables and their lags as inputs/predictors

Role of Environments







		Input	RMSE Fit/Pred	R^2 Fit/Pred
HONG KONG	ARIMA	LST (2,5), Rainfall (3), RH (1)	0.367 / 0.563	0.909 / 0.826
	NN	Mean Dew Pt (1),T mean (1), LST (4)	0.537 / 1.01	0.748 / 0.0394
MARICOPA	ARIMA	T mean (1,7)	0.547 / 0.812	0.931 / 0.922
	NN	Min RH (1), T mean (4), Solar Rad. (4)	0.608 / 1.089	0.820 / 0.754
NEW YORK CITY	ARIMA	Mean Dew Pt (4)	0.046 / 0.022	0.311 / 0.795
	NN	Tmax (1), Rainfall (3), Tmin (2)	0.044 / 0.039	0.731 / 0.584

- NN models show that ~60% of influenza variability in the US regions can be accounted by meteorological factors
- ARIMA model performs better for Hong Kong and Maricopa
  - Previous cases are needed
  - Suggests the role of contact transmission
- Temperature seems to be the common determinants for influenza in all regions
- Reasonably accurate prediction

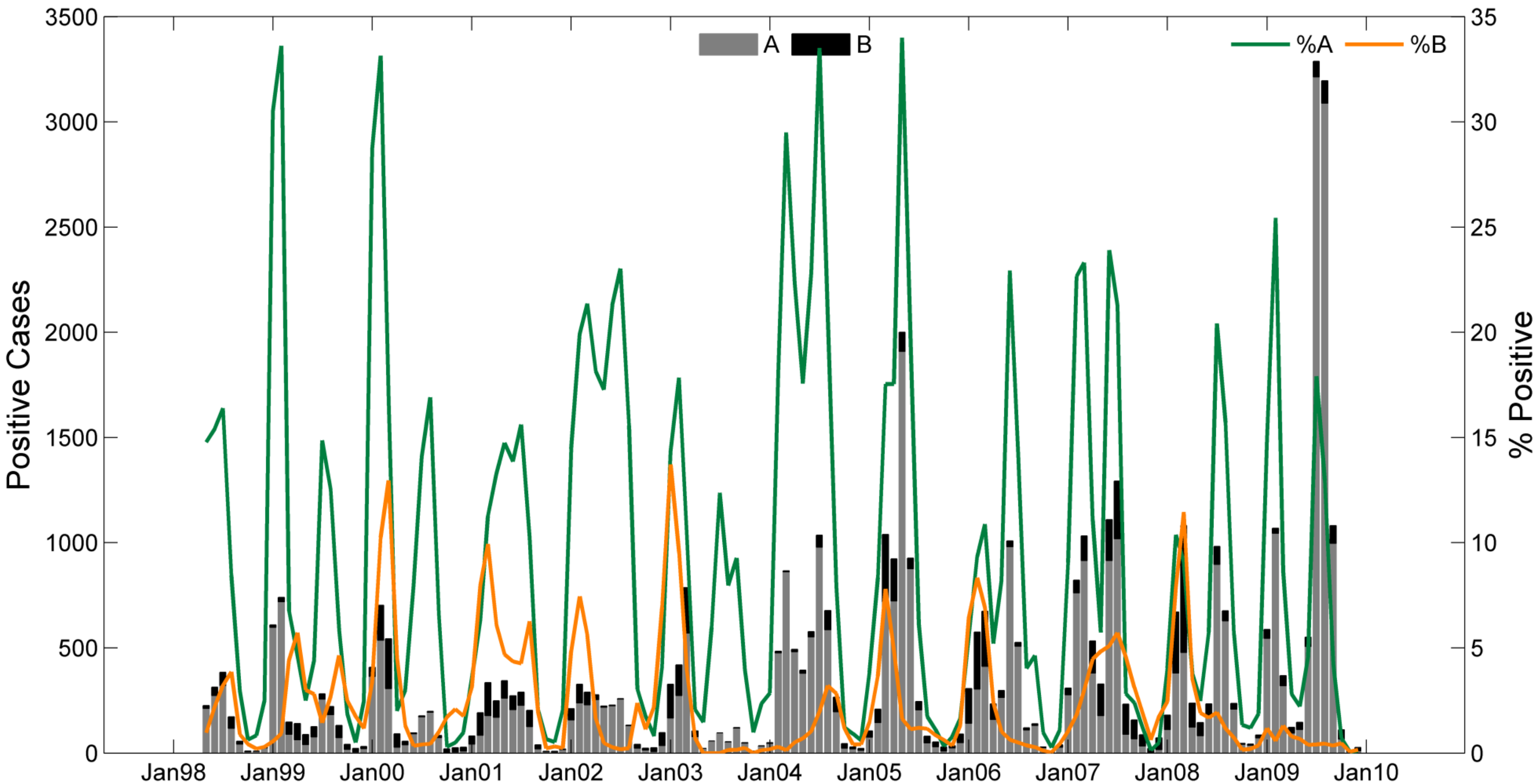
Role of Vapor Pressure

- Poisson regression model
- Vapor pressure included as input
- Improve model performance in temperate region

	Vapor Pressure excluded		Vapor Pressure included	
	RMSE	**R^2**	**RMSE**	**R^2**
Hong Kong	65.0037	0.593	74.188	0.478
Maricopa County	48.836	0.808	52.946	0.781
New York City	0.0248	0.66	0.0237	0.69

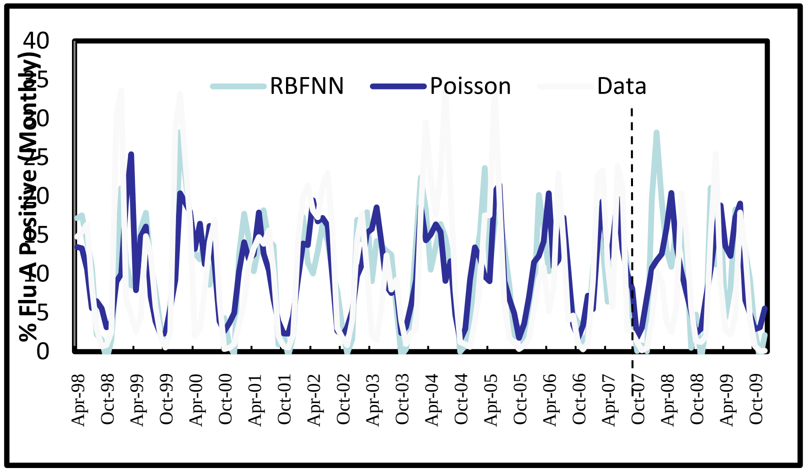
Environmental Sensitivity to Influenza Types and Subtypes

Hong Kong: Monthly Influenza A & B

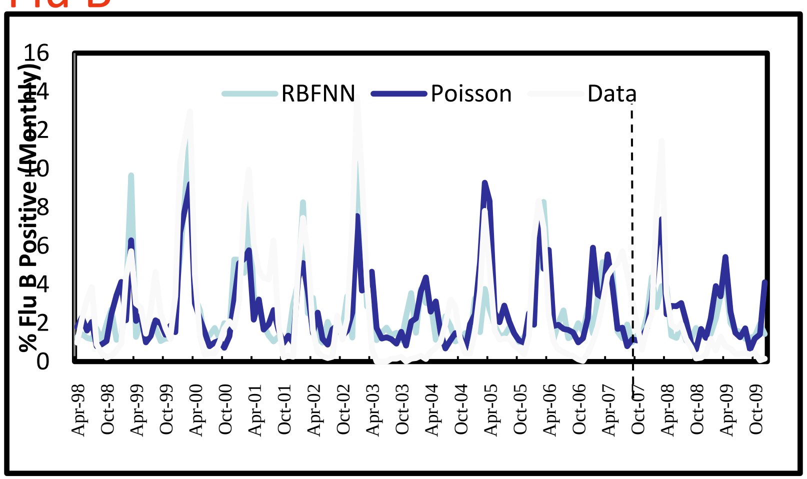


Influenza Types Sensitivity

Flu A



Flu B

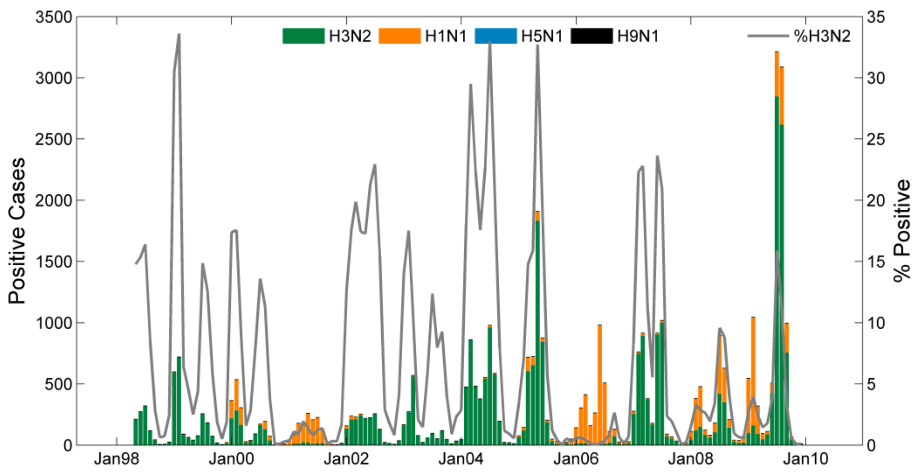


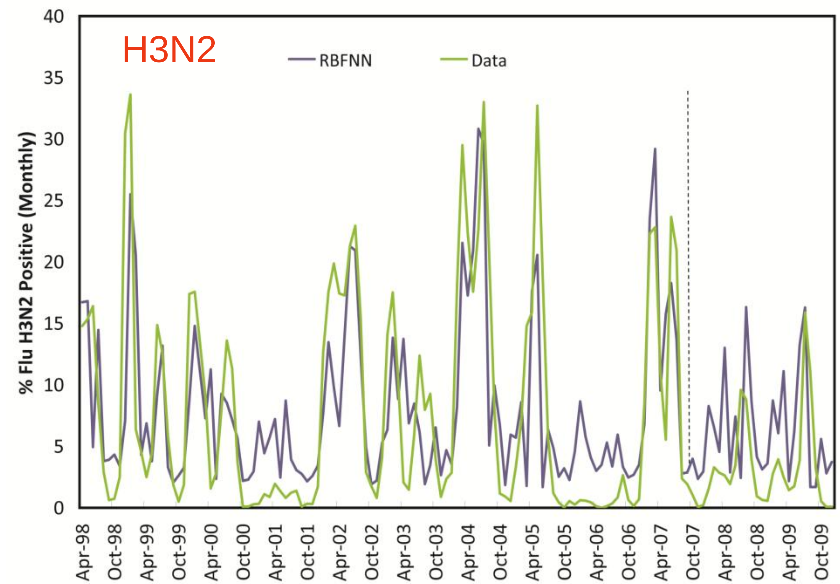
	Flu A	**Flu B**
Inputs	Mean Dew Pt., T min (2), Rainfall (3)	T max (1), Wind Speed, Flu B (2)
RMSE	6.432	1.825
R^2	0.497	0.594

- Flu A does not depend on the number of previous cases
  - Environments counts for ~50% of Flu A variability
- Flu B has dependency to previous cases

Influenza Subtypes Sensitivity

Hong Kong: Monthly Influenza A Subtypes



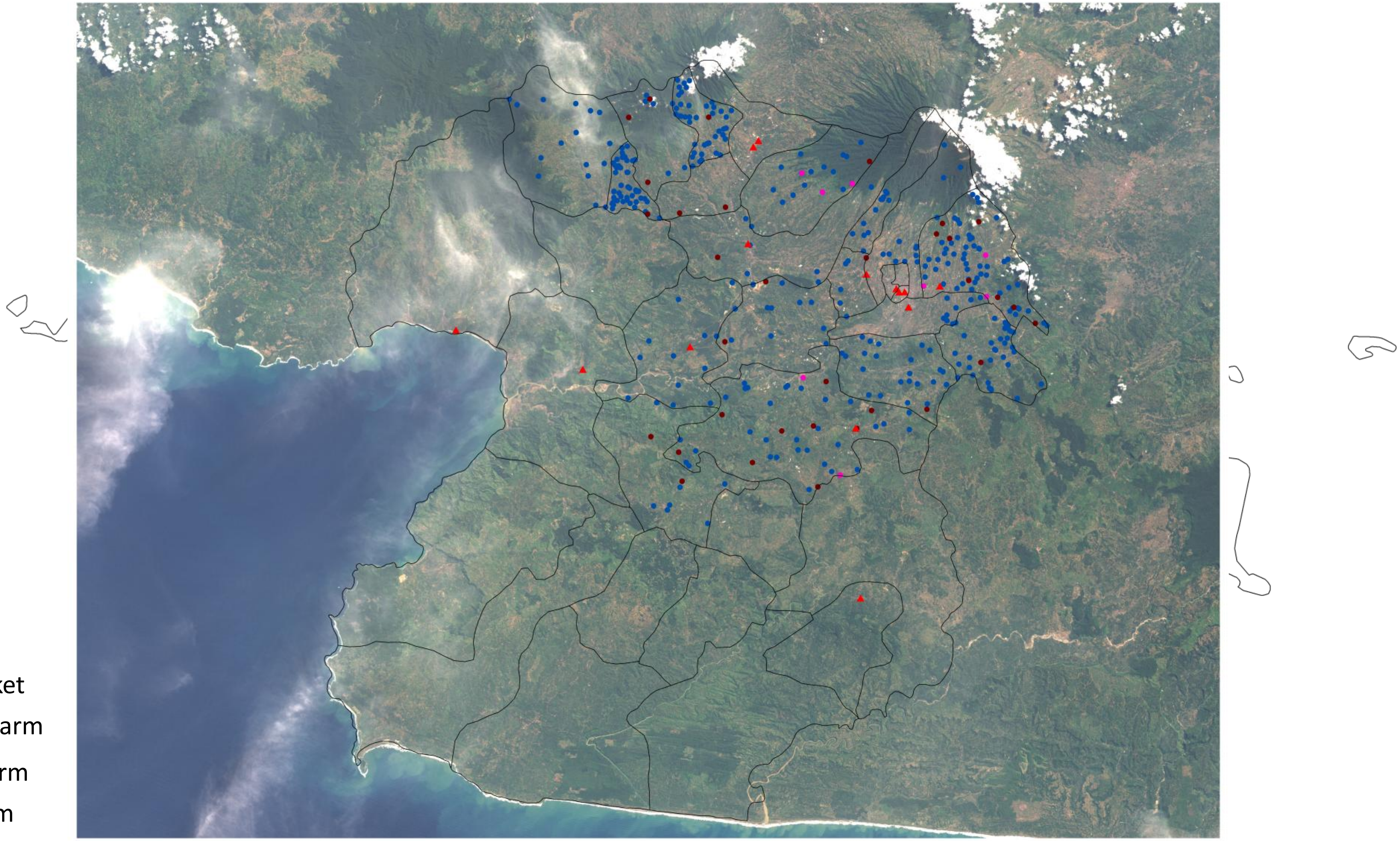


- Neural Network
  - Inputs: Mean Pressure (3), Sunlight (1), H3N2 Cases (1)
  - RMSE: 5.8766, R^2: 0.5662

Objective 3 – AI Spread
In Poultry Production and Trade

How do AI viruses spread on and off farms, within and across poultry sectors, and into the environment?

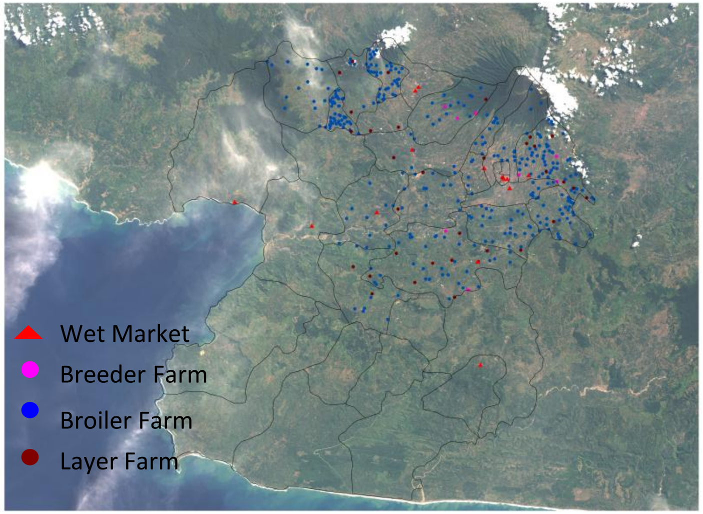
Farm Location

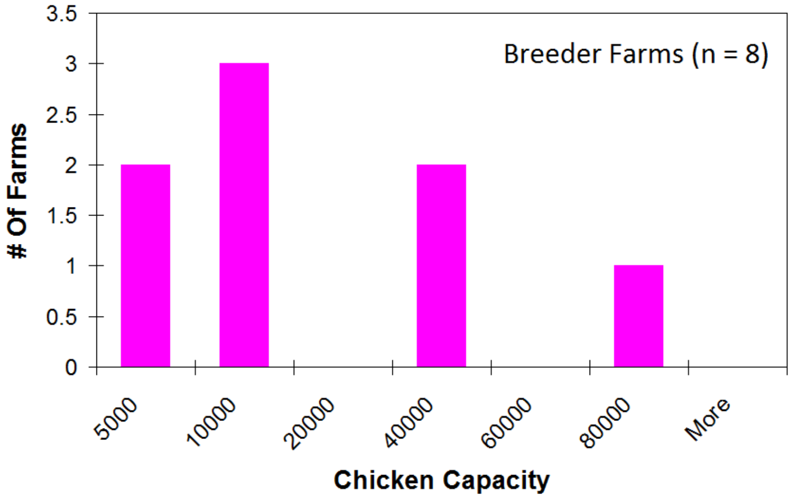


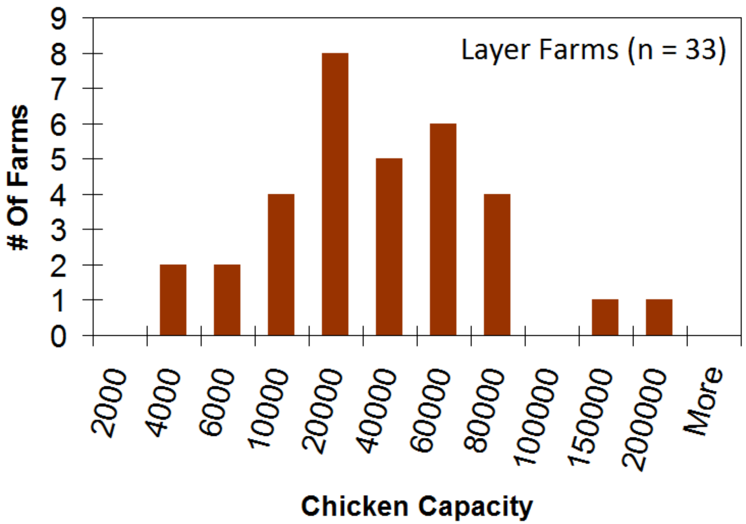
Wet Market
Breeder Farm
Broiler Farm
Layer Farm

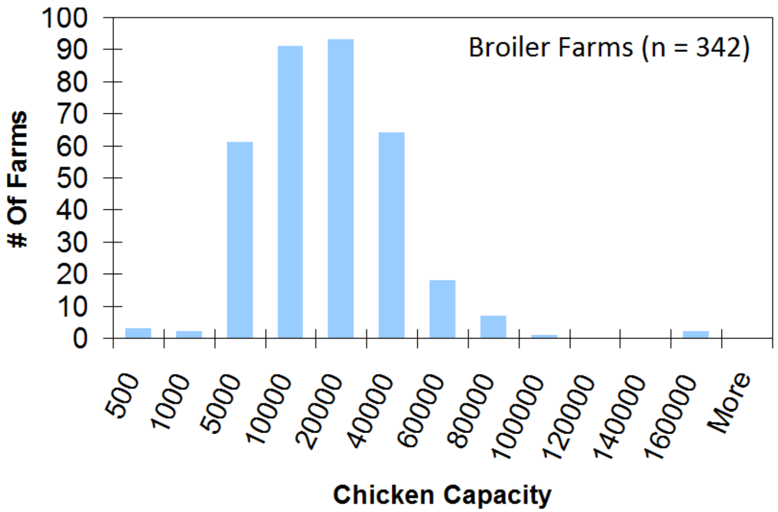
Sukabumi District, West Java

Chicken Capacity Distribution



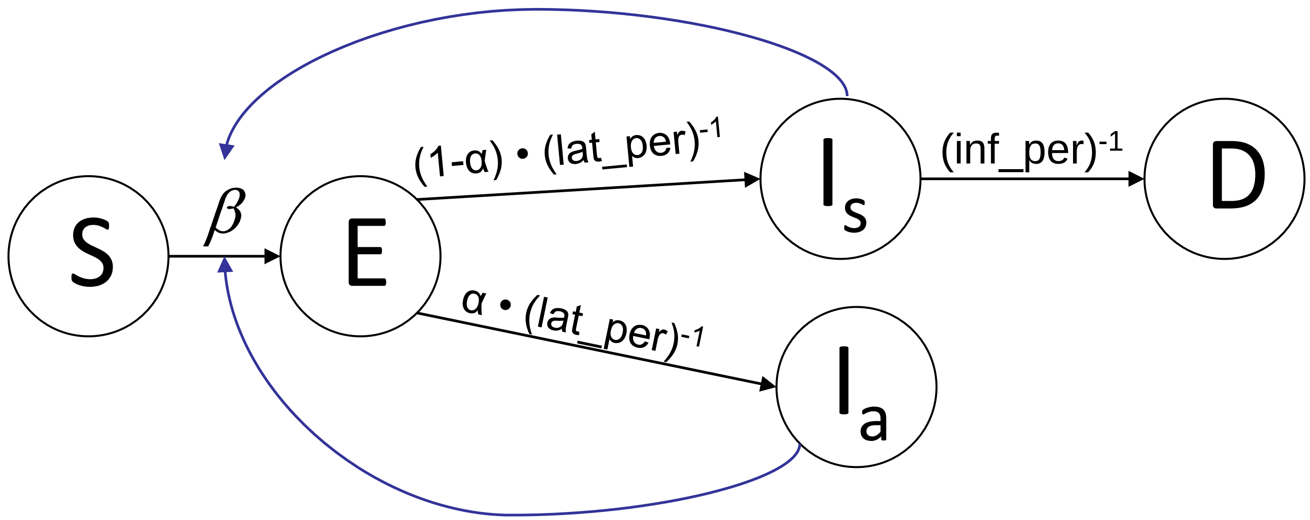






Within Farm Transmission

- Stochastic compartmental model



Variables:

S = Susceptible

E = Exposed

I_s = Infectious (symptomatic)

I_a = Infectious (asymptomatic)

D = Dead

Parameters (default value):

β = transmission rate (0.8)

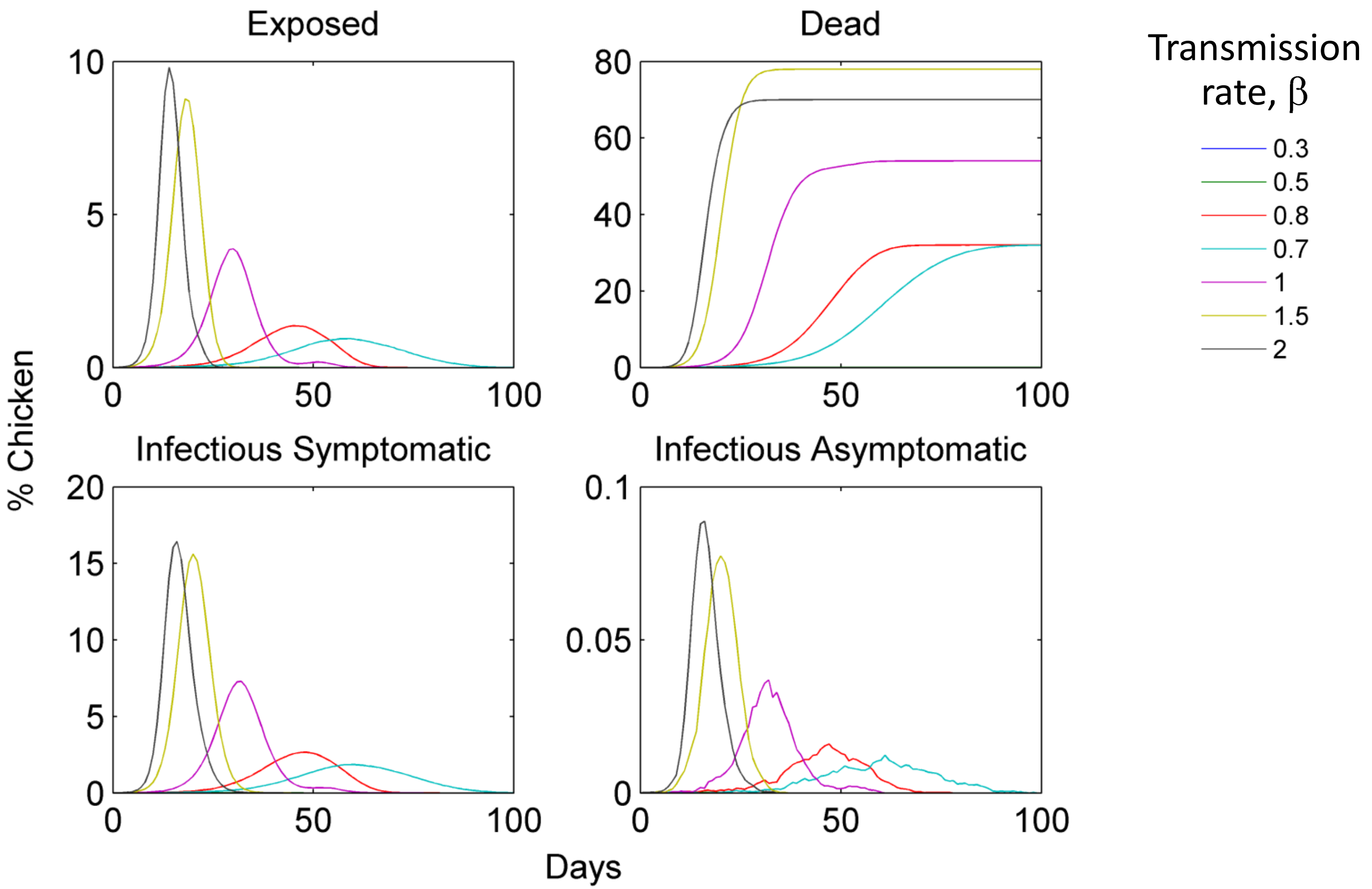
α = % asymptomatic (0.5%)

Lat_per = latent period (1 day)

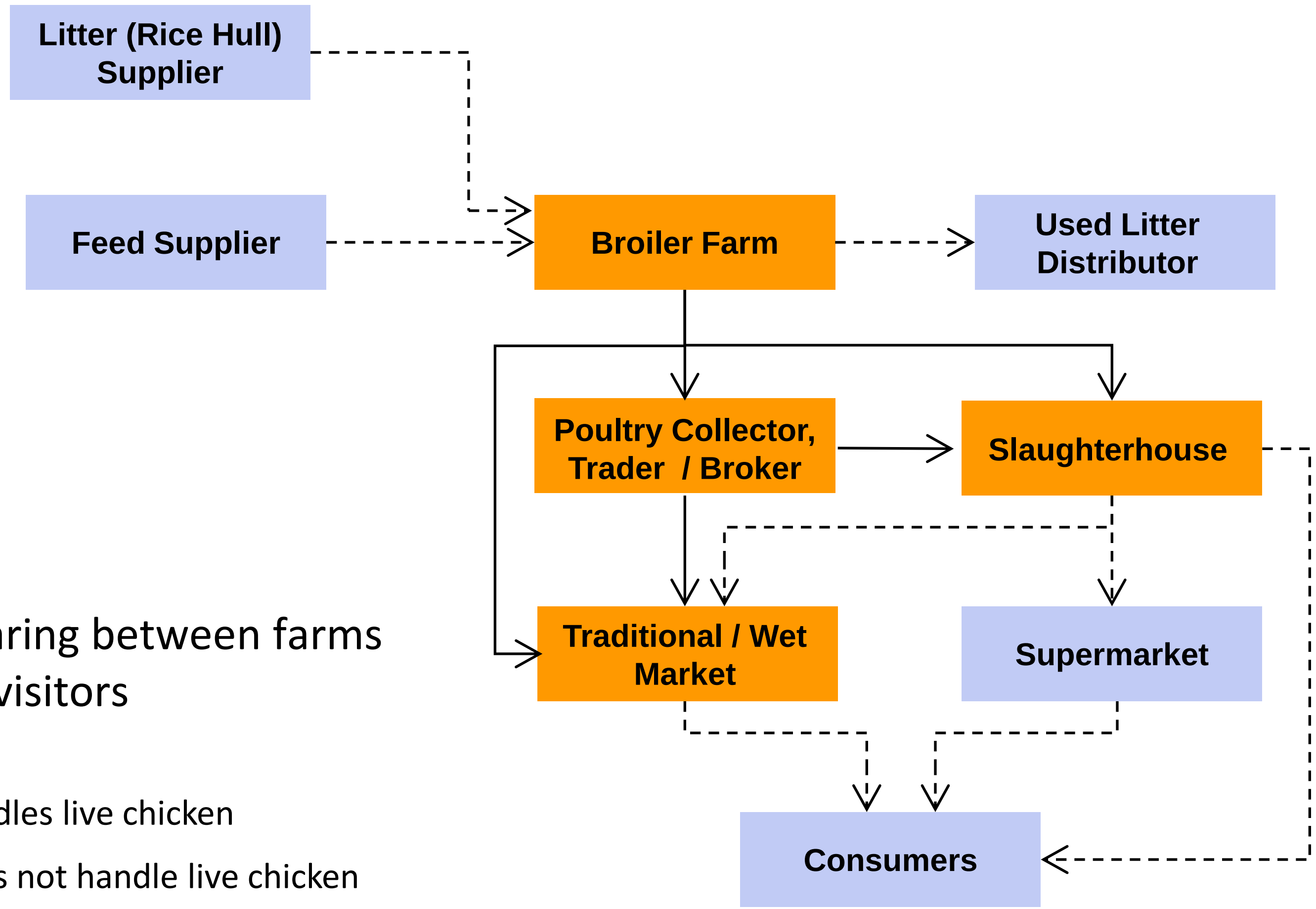
Inf_per = infectious period (2 days)

In-Farm Chicken State

- Chicken population with various transmission rate



Poultry Production Structure



Other contacts:

- Utilities
- Equipment sharing between farms
- Unauthorized visitors

Entity that handles live chicken

Entity that does not handle live chicken

Live chicken

Carcass or other materials

Between Farm Transmission

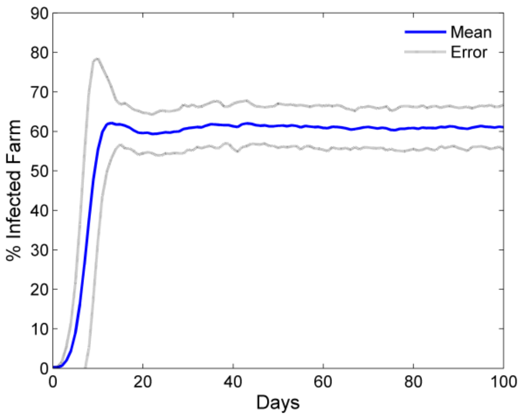
- Contacts considered in the simulation

	Risk Level	Visit period	Max # Farms visited/day
Feed trucks	Medium	10	3
Day Old Chick (DOC) Delivery	Medium	14	3
Selling chicken to collector/broker/wet market	Medium	7	3
Utilities	Low	3	10
Unauthorized visitor	High	1	4

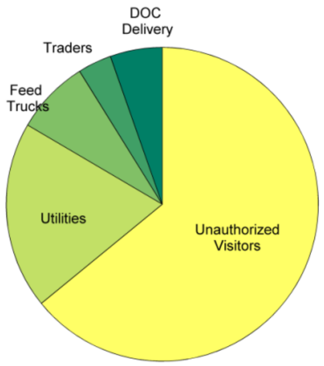
- Contact transmission rate takes into account the biosecurity level of the infected and susceptible farms
- Biosecurity level determined by the farm capacity
  - Larger farms tend to be more industrialized and have better biosecurity measures

HPAI Spread Between Farms

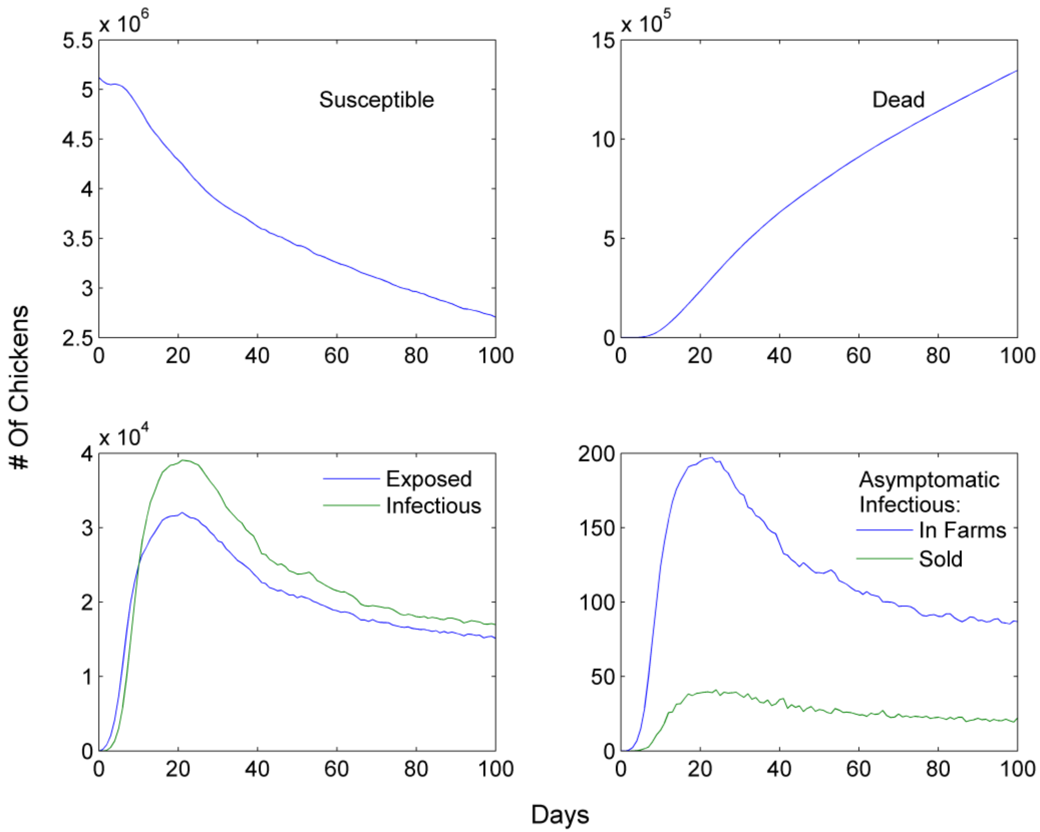
Number of farms that have at least one infectious chicken



Source of Infection



Chicken Population State In the District



FUTURE WORK

- Refine empirical AI outbreak model using additional environmental and socioeconomic parameters

- Continue the simulations of on- and off-farm, and within- and across-sector spread of H5N1 using scenarios provided by USDA and Cobb.

- Analyze the cross infection of influenza between poultry and swine if realistic scenarios can be obtained

- Continue the development of influenza predictive models using environmental and meteorological data as predictors for selected US and foreign population centers


Thank You!