A Stochastic Model of Avian Influenza H5N1 in Migratory Birds.

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- **Part VII:** Conclusion and future considerations

Avian Influenza

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- A year later, during the major poultry outbreak, the virus was found in humans in Hong Kong (1997).

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- Momentary changes happen in the direction of advection due to their seasonal behavior changes; such as predating animals.
- Interaction frequency among wild birds changes seasonally due to different cycles on social behaviour
- There are mainly two big stopover sites wintering and summer (breeding) locations.

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- **MOTIVATION:** Is that possible to apply a random perturbation to the dispersal movement of animals to eradicate/control AI?

Fisher's Equation

$$u_t = Du_{xx} + \lambda u(1-u) \qquad (1)$$

- First used by Ronald Fisher (Fisher-KPP equation) in 1937 to model diffusion of species in 1D habitat.
- Simplest nonlinear reaction diffusion equation
- Solution of the Fisher's equation generates traveling waves with minimum speed $C^*_{min} = 2\sqrt{\lambda D}$

Asymptotic solution generates a traveling wave

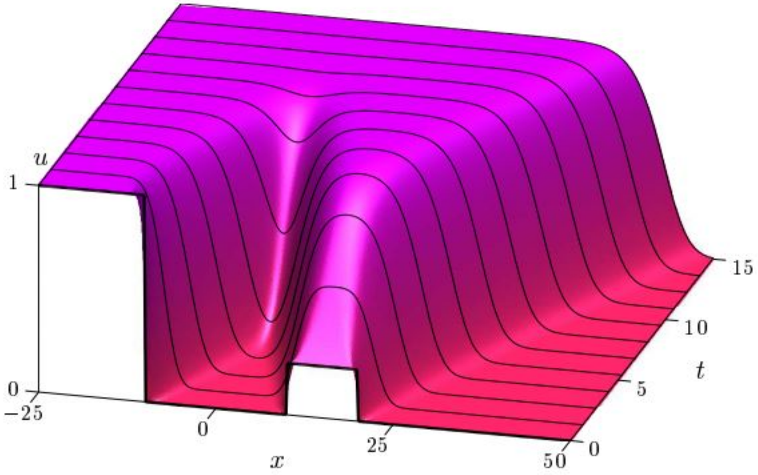


Fig. 1: Formation of traveling wave

Fisher-Kolmogorov-Petrovsky-Piskunov (KPP) Equation

$$\frac{\partial u}{\partial t} = A(x,t)\frac{\partial^2 U}{\partial x^2} + C(x,t)\frac{\partial u}{\partial x} + +B(x,t)u + H(x,t)u(1-u) \quad (2)$$

Eqn (2) is used to model the smooth heterogeneous problem, where H(x,t) is the nonuniform reaction term, and A(t)=1, B(t)=0, C(t)=0.

Stochastic SI Model with Time Dependent White Noise

$$\frac{dS}{dt} = -\beta I(1-I)$$
$$\frac{dI}{dt} = -\mu I + \beta I(1-I) + DI_{xx} + (\gamma(t) + \sigma \dot{W})I_x \quad I(0,x) = I_0(x)$$

β is the infection rate
μ is the death rate of infected birds
D is the diffusivity constant
$\gamma(t)$ is the advection coefficient.
σ is degree of dispersion in the noise of advection coefficient

Lemma-1

The stochastic Fisher equation with initial value problem has a solution $u(t,z) = U(t, X_t)$, such that $U(t,x)$ is the solution of

$$\partial_t U = \left(D - \frac{1}{2}\sigma^2\right)\partial_{xx} U + \beta U(1-U) - \mu U, \quad U(0,x) = \phi(x) \quad (3)$$

and X_t is the solution of

$$dX_t = \gamma(t)dt + \sigma dW_t, \quad (4)$$

with initial state $X_{t_0} = z$ and for $t \in [t_0, T]$.

Important Result of Lemma-1

Using the solution of the deterministic Fisher equation (3) and applying the suitable transformation to the stochastic process of X_t, we can find the solution of the stochastic SI equation, I(t,x).

Theorem-1

Immigration with Stochastic noise can eradicate epidemics. That is, with the appropriate selection of speed of immigration s.t.

$$I_t = DI_{xx} + \beta I(1 - I) - \mu I + (\gamma(t) + \sigma \dot{W}_t) I_x$$

and $I(0, x) = I_0$ *(non-random) where* $\dot{W}_t$ *is white noise. Let* $\lim_{t\to\infty} \frac{\int_0^t \gamma(s)ds}{t} = \gamma_0 \geq 0$ *and* $I^* = 1 - \frac{\mu}{\beta}$. *Then, The disease free equilibrium is going to be exponentially asymptotically stable almost surely.*

Proof of Theorem-1

For the equation below we assume that $\beta > \mu$:

$$I_t = (D - \frac{1}{2}\sigma^2)I_{xx} + \beta I(1 - I) - \mu I$$

Then let's introduce following parameters:
$d_0 = D - \frac{1}{2}\sigma^2$ and $I^* = 1 - \frac{\mu}{\beta}$ with the condition $d_0 > 0$ so the following equation arises:

$$I_t = d_0 I_{xx} + (\beta - \mu) I \left(1 - \frac{I}{I^*}\right).$$

With the transformation such that $T = d_0 t$, we get the following equation:

$$I_T = I_{xx} + \frac{(\beta - \mu)}{d_0} I \left(1 - \frac{I}{I^*}\right)$$

Then define M where $J = \frac{I}{I^*}$, we obtain

$$J_T = J_{xx} I^* + \frac{(\beta - \mu)}{d_0} J (1 - J).$$

Let $\rho = \frac{(\beta - \mu)}{d_0} > 0$ and the solution for our equality is given by EqWorld.

$$I(t, x) = I^* J(t, z) = I^* \left[\frac{1}{1 + \exp\left(\sqrt{\frac{\rho}{6}} z - \frac{5\rho}{6} d_0 t \right)} \right]^2$$

where $z = x + \sigma W_t + \int_0^t \gamma(s) ds$ Therefore, we have that

$$log(I) = log(I^*) - 2log \left(1 + \exp \left(\sqrt{\frac{\rho}{6}} \left(x + \sigma W_t + \int_0^t \gamma(s) ds \right) \right.\right.$$

$$\left.\left. - \frac{5\rho}{6} d_0 t \right) \right)$$

$$\log(I) =$$
$$\mathit{log}\left(I^*\right) - 2\mathit{log}\left(1 + \exp\left(\sqrt{\frac{\rho}{6}}\left(x + \sigma W_t + \int_0^t \gamma(s)ds\right) - \frac{5\rho}{6} d_0 t\right)\right)$$
$$\log(I) \leq \mathit{log}\left(I^*\right) - 2\left(\sqrt{\frac{\rho}{6}}\left(x + \sigma W_t + \int_0^t \gamma(s)ds\right) - \frac{5\rho}{6} d_0 t\right)$$
$$\log(I)/t$$
$$\leq \frac{\mathit{log}\left(I^*\right)}{t} - 2\sqrt{\frac{(\beta-\mu)}{6d_0}}\left(\frac{x}{t} + \frac{\sigma W_t}{t} + \frac{\int_0^t \gamma(s)ds}{t}\right) + \frac{5}{3}(\beta - \mu).$$

Now, by taking the limit supremum as $t \to \infty$ we obtain ($\lim\limits_{t\to\infty} \frac{W_t}{t} = 0$ a.s. by Strong Law of Strong Numbers for Brownian motion.)

$$\limsup_{t\to\infty}\frac{log(I)}{t} \leq \frac{5}{3}(\beta-\mu) - 2\sqrt{\frac{(\beta-\mu)}{6d_0}}\gamma_0.$$

This implies that the stochastic endemic equilibrium is still exponentially stable contrary to the deterministic endemic equilibrium if

$$\triangle = \frac{5}{3}(\beta-\mu) - 2\sqrt{\frac{(\beta-\mu)}{6d_0}}\gamma_0 < 0$$

$\widetilde{R} = \frac{\beta}{\mu+\frac{6}{25}\cdot\frac{\gamma_0^2}{d_0}} < 1.$

Results: Example

$\frac{dI}{dt} = 3\partial_{zz} I(t,z) + (25 - \sin(t))\partial_z I(t,z) + I(t,z)\,(1 - I(t,z)) -$
$(0.1)I(t,z) + \partial_z I\, dW_t,$
where,
I(0,z)= $\dfrac{1}{\left[1 + \exp(\sqrt{\frac{3}{50}}z)\right]^2}$ for $t \in [0,1]$.

By Lemma-1, equation has a solution $I(t,z) = (I^*)U(t,X_t)$, such that $U(t,x)$ is the solution of

$$\partial_t U = (2.5)\partial_{xx} U + U(1-U) - (0.1)U, \quad U(0,x) = \frac{1}{\left[1 + \exp(\sqrt{\frac{3}{50}}x)\right]^2} \tag{5}$$

and X_t is the solution of

Results: Example, continues

$dX_t = (25 - \sin(t))dt + dW_t,$
with initial state $X_0 = z$ and for $t \in [0, 1]$.
By Suazo's work, U(t,x) has the following solution

$$U(t, x) = \left[\frac{1}{1 + \exp\left(\sqrt{\frac{3}{50}}x - \frac{3}{4}t\right)} \right]^2$$

for $x \in \mathbb{R}$.
The stochastic equation has a solution given by

$$X_t = z + W_t + \int_0^t 25 - \sin(s)ds$$

for $t \in [0, 1]$.

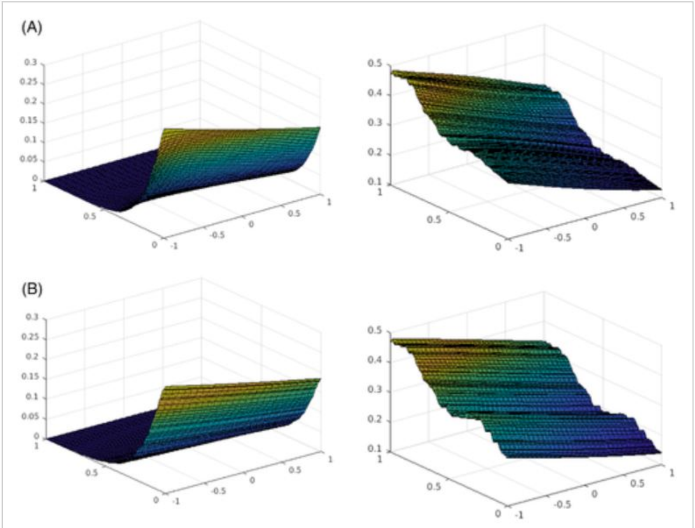
Results: Example, continues

Therefore, the general solution of the stochastic Fisher equation is given by

$$I(t,z) = I^* \left[\frac{1}{1+\exp\left(\sqrt{\frac{3}{50}}\left(z + W_t + \int_0^t 25 - \sin(s)ds\right) - \frac{3}{4}t\right)} \right]^2 \tag{6}$$

for $t \in [0,1]$ and $z \in \mathbb{R}$.

Results: Numerical approximation and exact solution are represented by (A) and (B), respectively.



Numerical method/Iterative Method

- To solve the partial differential equation on the stochastic mesh, the algorithm uses time discretization by finite difference and Runge-Kutta method, and central difference for space. We call the last scheme RKCD.

Algorithm

- Discretize $[t_0, T]$ into a time line space $DT : t_0, t_1, \ldots, t_m = T$ and discretize space $[a, b]$ into $DS : a = z_0, z_1, \ldots, z_n = b$

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- For each $j = 1, \ldots, n$ we solve for $X_{t_0} = z_j$ using RKM-1.5 resulting in $x_{i(j)} := X_{t_i}(z_j)$ with $i = 0, 1, \ldots, m$. This step will result in a stochastic mesh $\{(t_i, x_{i(j)}) : i = 0, \ldots, m; j = 0, \ldots, n\}$.

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- Use a finite (central) difference for time and space in the deterministic partial differential equation and then use RKCD to solve a first order ODE boundary value problem with boundaries at $x_{i(0)}$ and $x_{i(n)}$, for all $i = 1, \ldots, m$.

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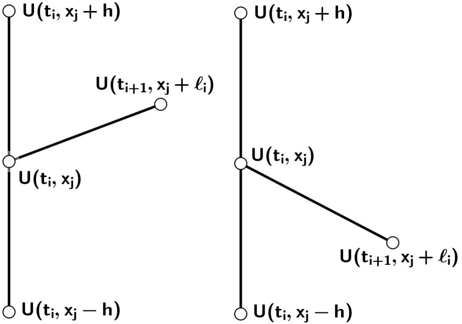
- Use a finite (central) difference for time and space in the deterministic partial differential equation and then use RKCD to solve a first order ODE boundary value problem with boundaries at $x_{i(0)}$ and $x_{i(n)}$, for all $i = 1, \ldots, m$.
- The approximate solution of the stochastic Fisher equation $u(t_i, z_j) = U(t_i, x_{i(j)})$ for $i = 1, \ldots, m$ and $j = 1, \ldots, n$.

Solving PDEs on a Stochastic Mesh

The numerical scheme uses the stencil in the figure below. If the space coordinate on the mesh is $x_{i(j)} = x_j$, then $x_{i+1(j)} := x_j + \ell_i$.



Stencil of the numerical scheme with the realization of the incremental trajectory dX_t when it is positive (right) and negative (left). The stencil is shown for $\Delta t = k$ and $\Delta x = h$ which are fixed.

The bi-variate Taylor expansion of $U(t+k, x+\ell)$ about (t, x) gives the following approximations

$$U(t+k, x+\ell) - U(t,x) \approx k\partial_t U(t,x) + \ell\partial_x U(t,x) + \frac{1}{2}\ell^2\partial_{xx}U(t,x)$$

and

$$U(t, x \pm h) - U(t,x) \approx \pm h\partial_x U(t,x) + \frac{1}{2}h^2\partial_{xx}U(t,x)$$

or equivalently

$$\begin{bmatrix} h & \frac{h^2}{2} & 0 \\ -h & \frac{h^2}{2} & 0 \\ \ell & \frac{\ell^2}{2} & k \end{bmatrix} \cdot \begin{bmatrix} \partial_x U(t,x) \\ \partial_{xx} U(t,x) \\ \partial_t U(t,x) \end{bmatrix} = \begin{bmatrix} U(t, x+h) - U(t,x) \\ U(t, x-h) - U(t,x) \\ U(t+k, x+\ell) - U(t,x) \end{bmatrix}.$$

Thus,

$$\partial_x U(t,x) = \frac{U(t,x+h) - U(t,x-h)}{2h},$$

$$\partial_{xx} U(t,x) = \frac{U(t,x+h) - 2U(t,x) + U(t,x-h)}{h^2},$$

and

$$\partial_t U(t,x) = \frac{U(t+k,x+\ell) - U(t,x)}{k} - \frac{\ell}{k}\partial_x U(t,x) - \frac{\ell^2}{2k}\partial_{xx} U(t,x).$$

These equations lead to the iterative scheme

$$U(t_{i+1}, x_{i+1(j)}) = U(t_i, x_j) + k \Bigg[(A(t_i) - \frac{1}{2}E^2(t_i) + \frac{\ell_i^2}{2k})$$

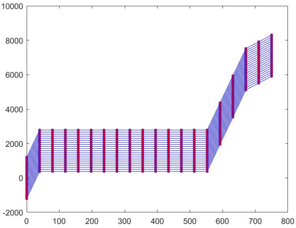
$$\times \frac{U(t_i, x_j + h) - 2U(t_i, x_j) + U(t_i, x_j - h)}{h^2}$$

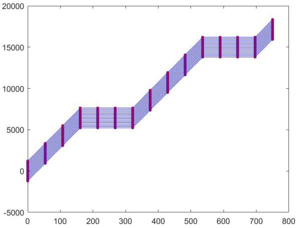
$$+B(t_i)\frac{U^2(t_i, x_j + h) - U^2(t_i, x_j - h)}{4h} + \frac{\ell_i}{k}\frac{U(t_i, x_j + h) - U(t_i, x_j - h)}{2h}$$

$$+D(t_i)U(t_i, x_j)]$$

starting with $U(t_0, z_j) = \phi(z_j)$, where $\ell_i = x_{i+1(j)} - x_{i(j)}$, $h = z_{j+1} - z_j$, and $k = t_{i+1} - t_i$.

Samples of stochastic meshes



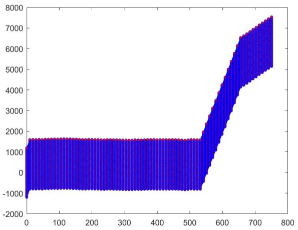


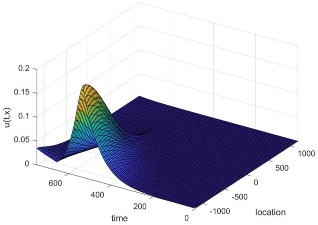
These stochastic meshes are generated for different Δx and Δt values to solve the stochastic fisher equation for D=250, $\beta = 5.5$, $\mu = 1.5$, $\sigma = 3$

Figure on left: The space and time intervals are divided by 20 sub intervals

Figure on right: The space and time intervals are divided by 15 sub intervals

Solution curve along with a given stochastic mesh





Summary and conclusions

- Important condition is found to stabilize the stochastic fisher equation, so to eradicate the disease.
- Future work includes working with the real migration and AI influenza case data to help health officers for finding best methods to stop/eradicate the spread of AI.
- Some challenges are; estimating diffusion coefficient, finding parameters depending on the yearly migration behaviour, etc.

Avian Influenza Birds to Human Model

Human population is divided into three groups as susceptible, infected, and recovered humans with the size H, C, and R.

$$\frac{dI(t,x)}{dt} = -\mu I(t,x) + \beta I(t,x)(1 - I(t,x)) + D I_{xx}(t,x) + (\gamma(t) + \sigma \dot{W}) I_x(t,x$$

$$\frac{dH(t,x)}{dt} = \lambda - \alpha H(t,x) - \beta_1 H(t,x) I(t,x)$$

$$\frac{dC(t,x)}{dt} = \beta_1 H(t,x) I(t,x) - (\alpha + \xi) C(t,x) - \theta C(t,x)$$

$$\frac{dR(t,x)}{dt} = \theta C(t,x) - \alpha R(t,x)$$

Parameter Estimations

Parameter Description	Symbol	Value
Death rate in wild birds	μ	0.01
AI transmission rate in wild birds	β	1.5
Diffusivity rate of infected birds	D	computed
Advection coefficient	γ	computed
Degree of dispersion	σ	computed
Natural birth rate for susceptible human	λ	100
Natural death rate for H and C	α	0.39
AI related death rate for infected human	ξ	0.3
AI transmission rate to human.	β_1	0.8
AI recovery rate for infected human.	θ	100

Estimating D

$$D = \frac{\sum_{i=1}^{n} l_i^2}{\sum_{i=1}^{n} t_i} \tag{7}$$

Migration	Mean travel dist (km)	Mean travel time (days)
Wintering period	636	12
Molt migration	1765	24.5
Spring migration	2987	67

Table: Mean travel distance and time for migratory birds

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Thank You

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