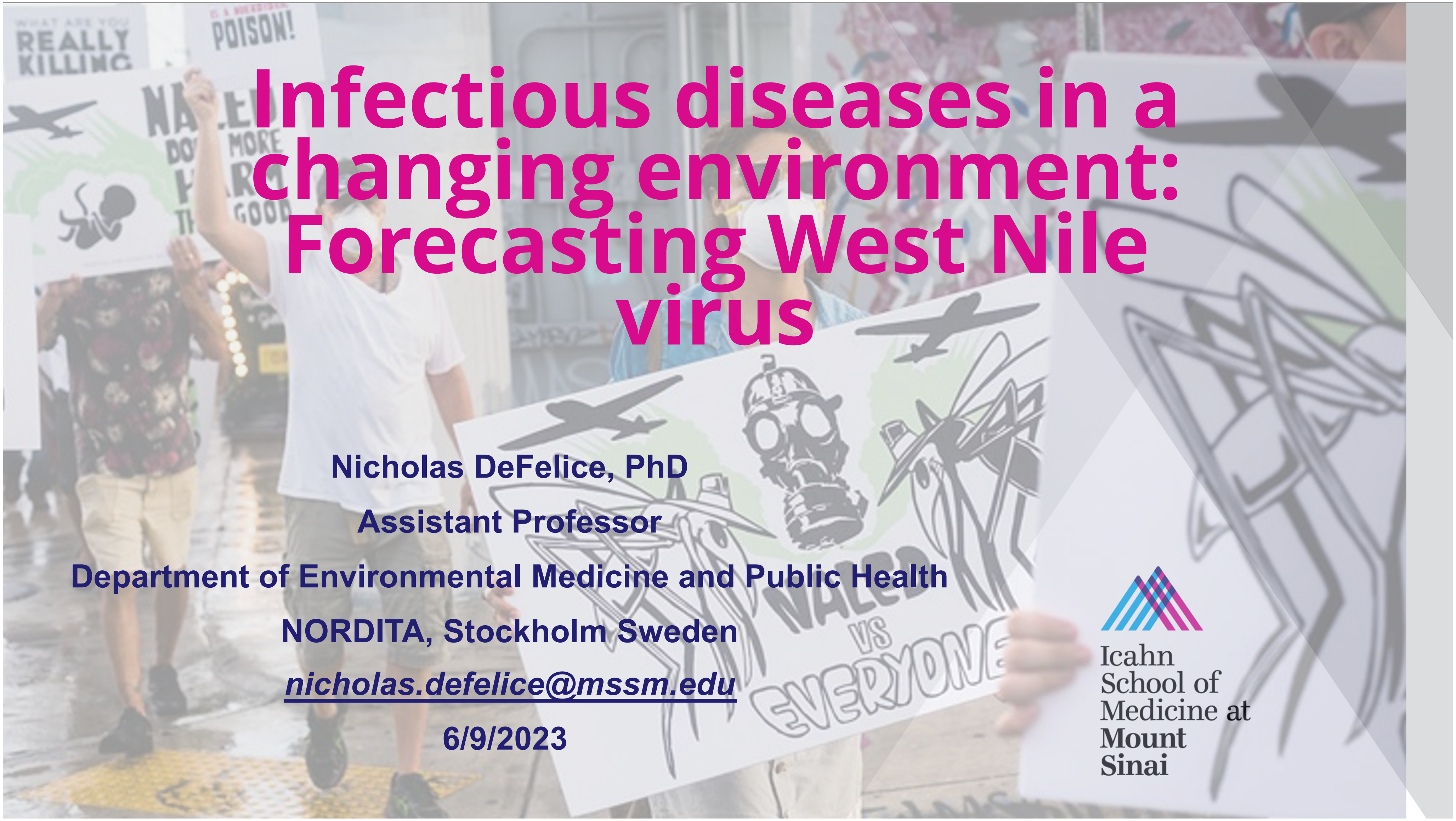


Infectious diseases in a changing environment: Forecasting West Nile virus

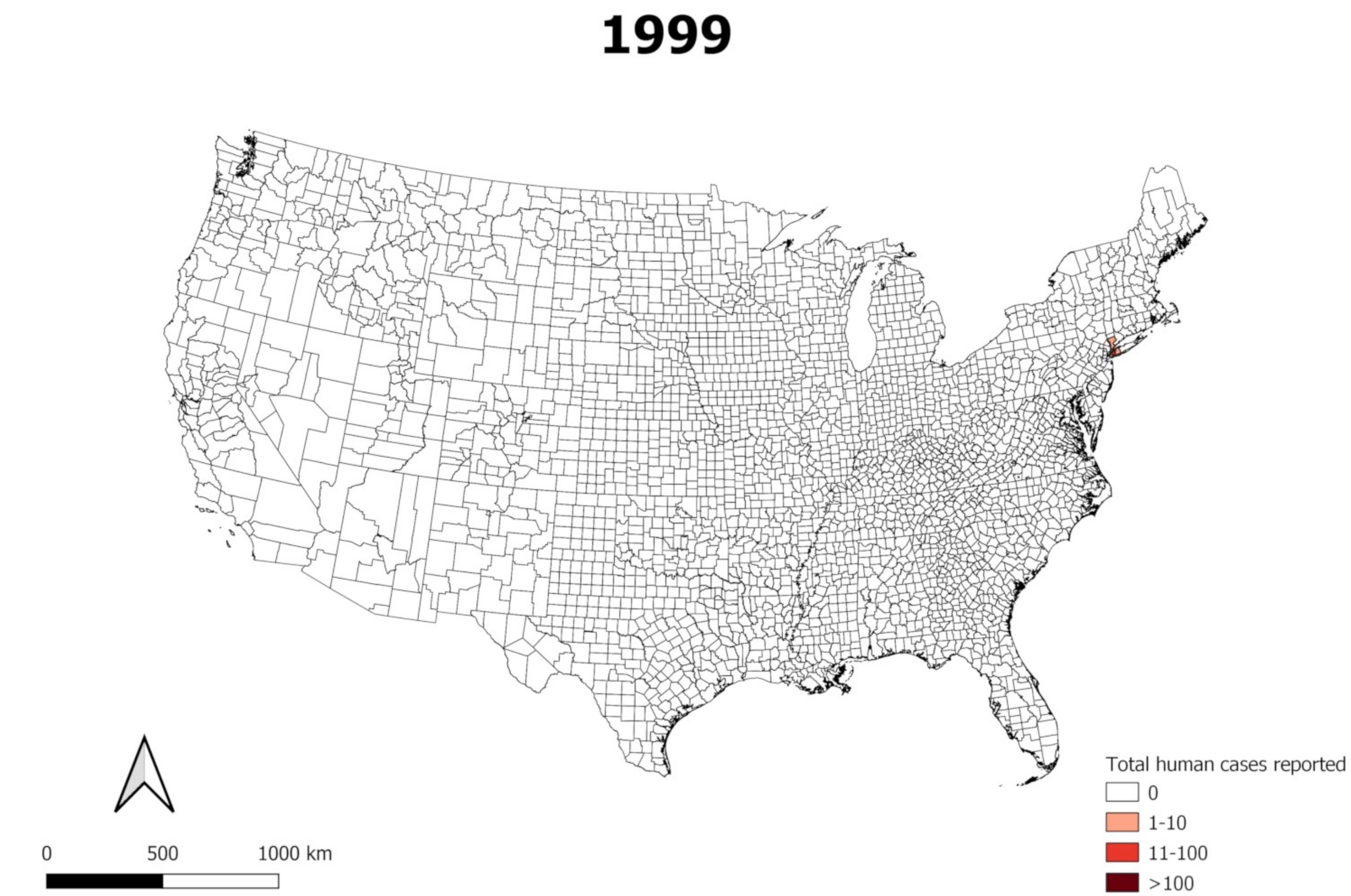
Nicholas DeFelice, PhD
Assistant Professor
Department of Environmental Medicine and Public Health
NORDITA, Stockholm Sweden
nicholas.defelice@mssm.edu

6/9/2023

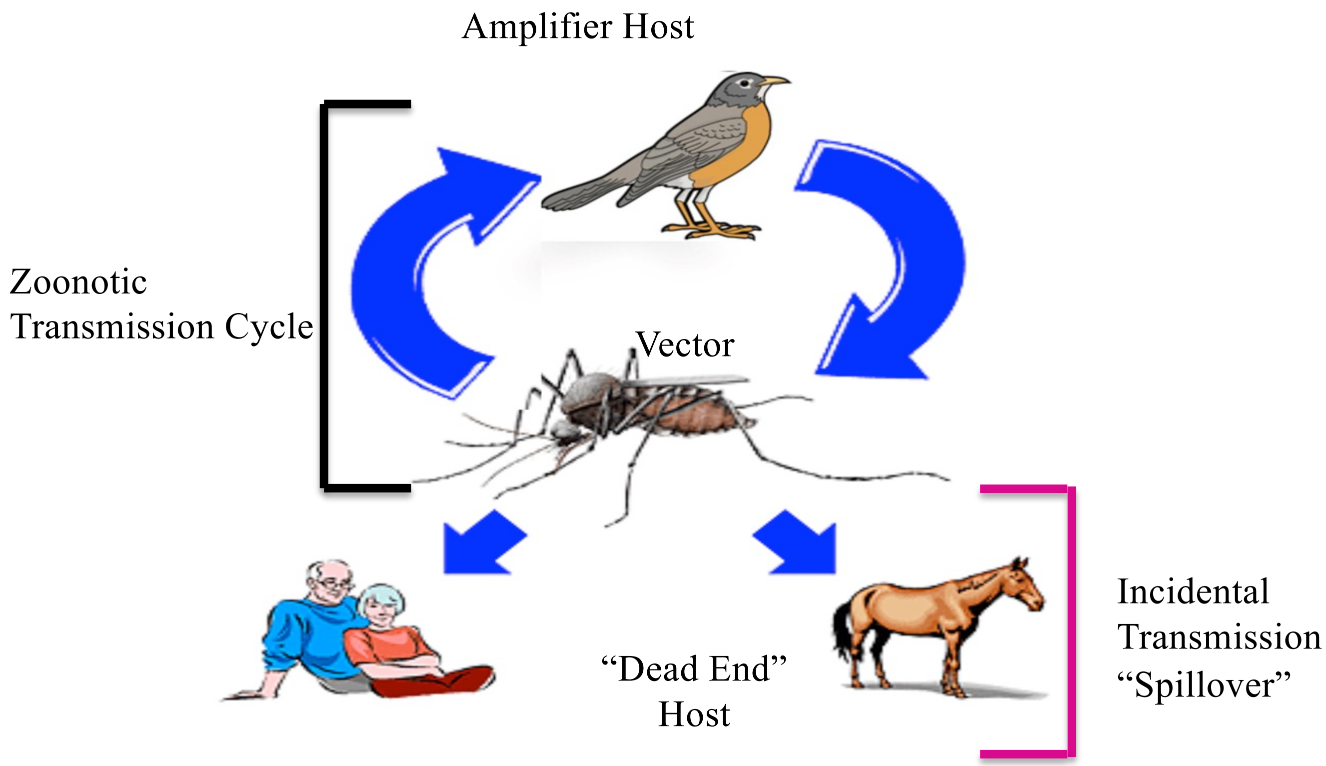
Icahn School of Medicine at Mount Sinai

WNV in the United States

- Spatial & temporal variability
- Even in low transmission years there are portions of the country with high incidence



West Nile Virus Transmission Cycle



Background

Hydrology/Precipitation Contradictory

- Rainfall
  - Near-surface humidity, enhances mosquito flight activity and host-seeking behavior
  - Can increase breeding sites[1]
- Heavy rain
  - Decrease larval survival though flushing and consequently reduce the vector population[2]
- Drought
  - More water used at home increase potential exposure
  - Reduced predators[3]
  - Pushed birds and mosquitoes together creating optimal conditions for WNV amplification[4]

[1]Shaman & Day 2007; [2]Koenraadt & Harrington;[3]Chase & Knight 2003; [4]Shamanet et al. 2005

Background

Humidity

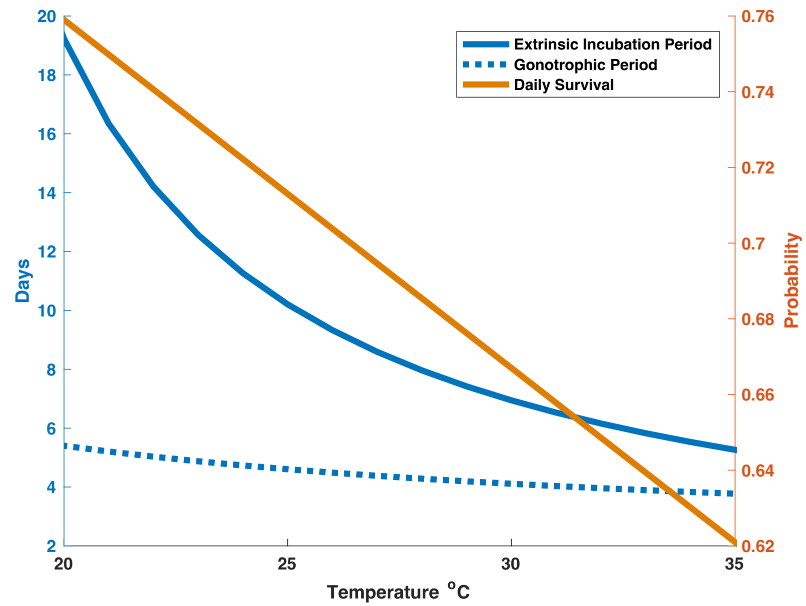
- Positively correlated with an increase in host-seeking behavior and mosquito population dynamics[1-3]
- Small arthropods have high surface area to body volume and easily lose moisture through evaporation
- They have waxy layer on external cuticle to limit water loss but it still occurs through respiration and defecation
- Prefers 60- 80% relativity humidity, shows signs of stress < 40%

[1]Paz, 2006; [2] Paz et al. 2013; [3]Walsh et all 2008

Background

Temperature

- Influence mosquito development rates
- Shorten the duration of the gonotrophic period[1]
  - time interval between host-seeking activity
- Decrease the extrinsic incubation period of the virus[2-5]
  - virus to develop more quickly
- Warmer temperature decreases vector survival[6]

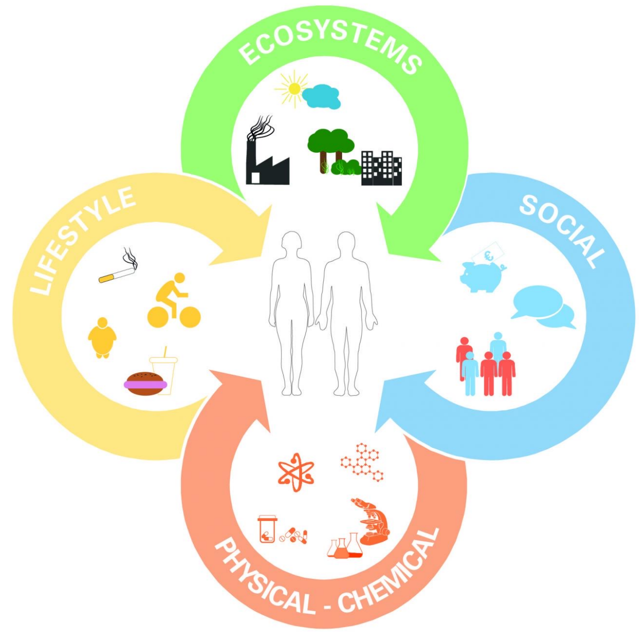


[1]Reisen et al. 1992; [2]Hartley et al. 2012; [3]Reisen et al. 2006; [4]Richards et al. 2007; [5]Kilpatrick et al. 2008; [5]Mordecai et al. 2013

Background

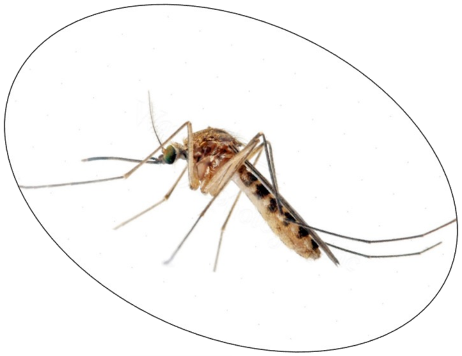
Prevention

- No human vaccine or specific treatment
- Personal protection
  - Mosquito repellent
  - Long sleeve shirts and pants
- Community based mosquito control programs

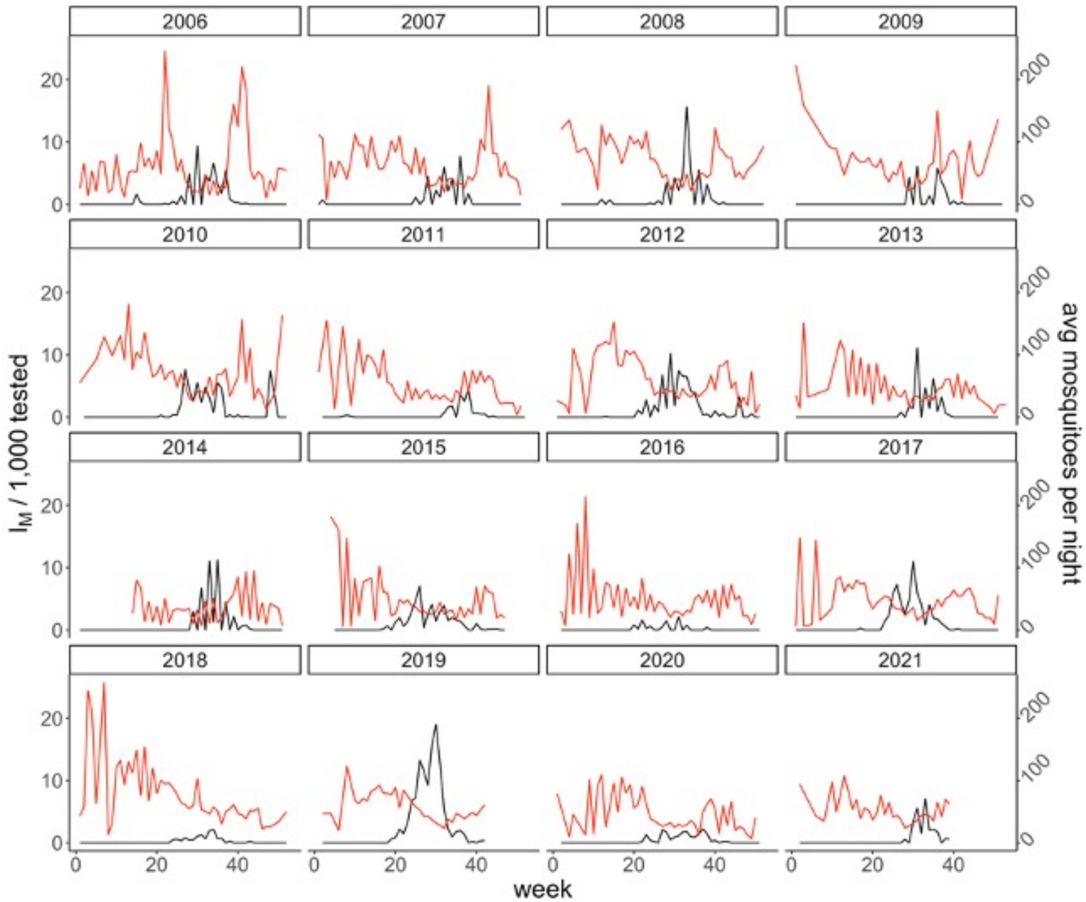


Public health decision support tools

- Infectious disease patterns continually shift
- Within infectious disease outbreak, response is reactive
  - Based on ongoing surveillance
- Accurate, reliable forecasts with sufficient lead times would provide greater opportunity to plan adaptive mitigation and control efforts

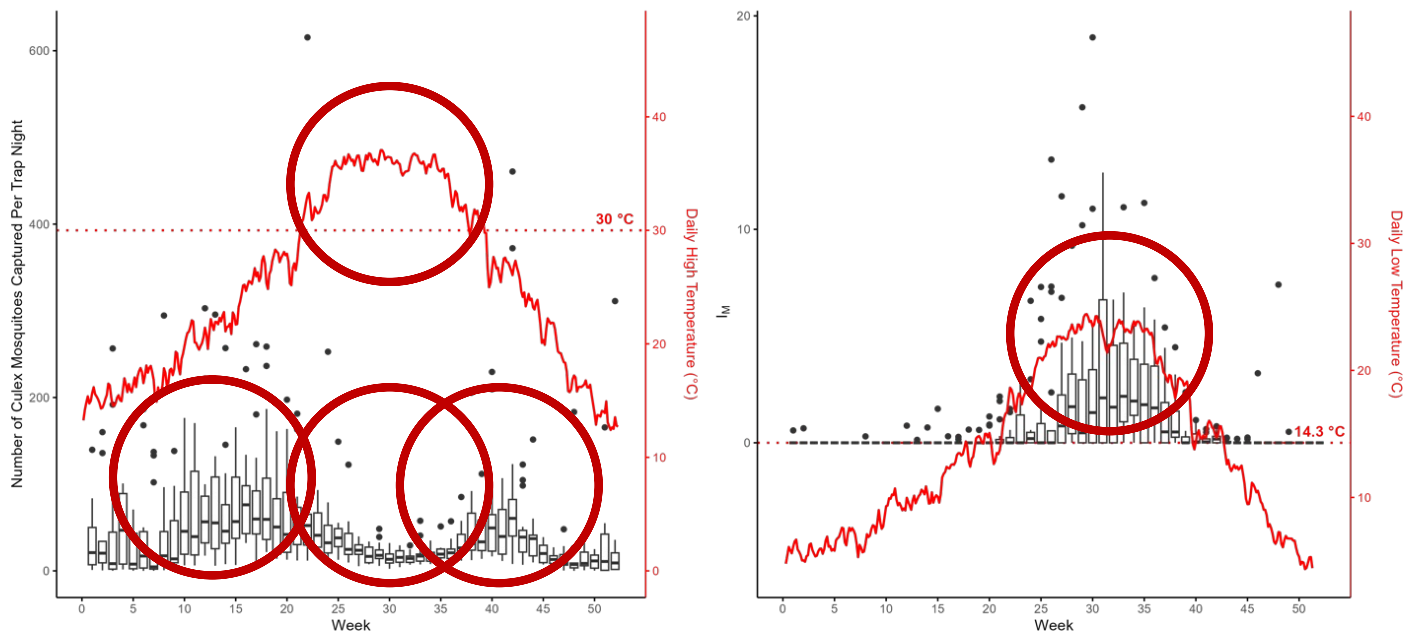


Temporal variability of Mosquito infection rates



Climatology & Mosquito Population

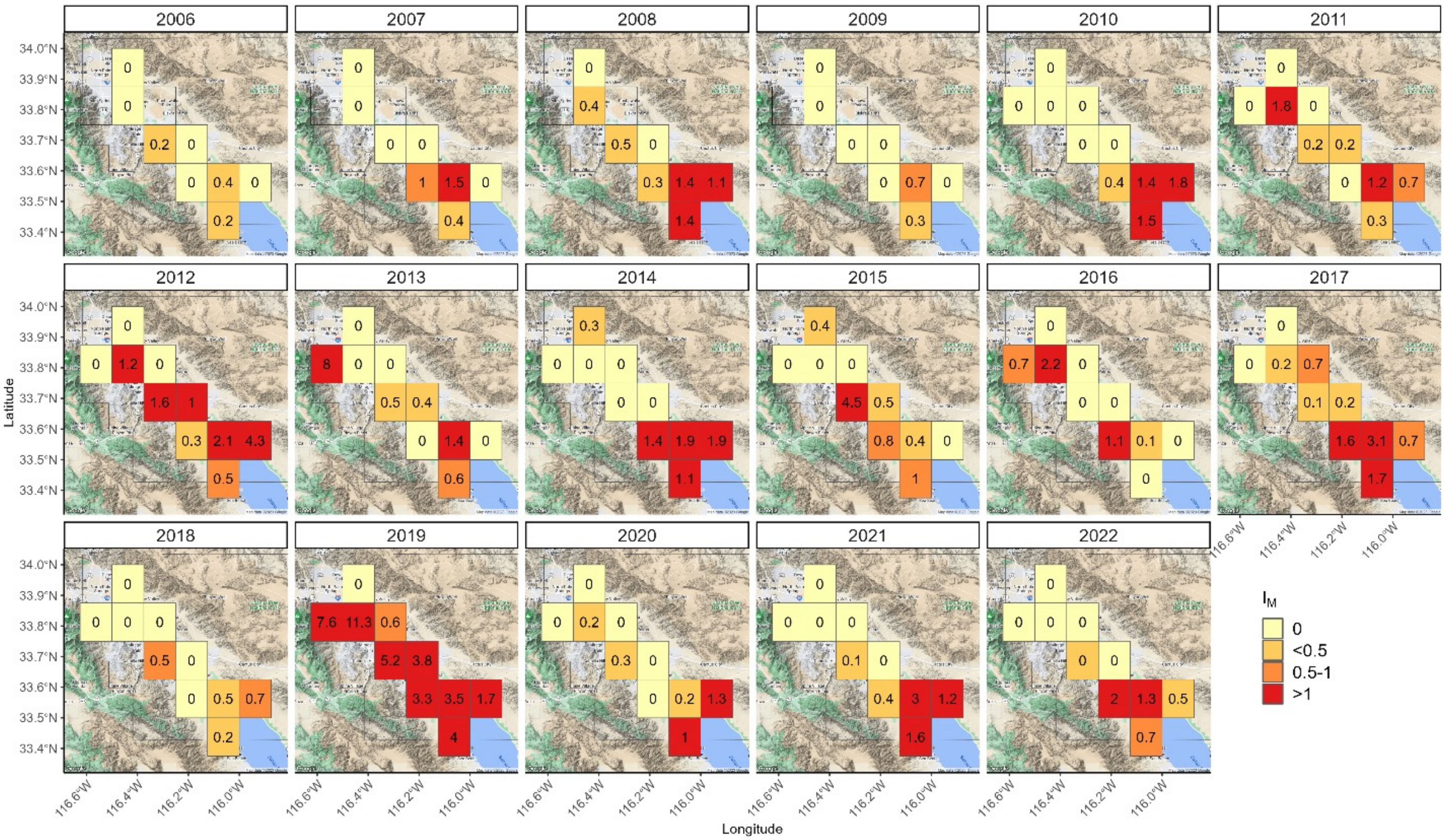
- Mosquito population normalized by trap night
- Pronounced bimodal structure
- Conversely, the I_M peaks during the summer
- Annual variability in these trends was observed.



Historical CV *Culex* mosquito abundance, I_M and ATMP between 2006 - 2022. Left: Weekly mean number of mosquitoes trapped per night (boxplot, dots = outliers > 2*SD), maximum daily ATMP (red line), and temperature threshold for mosquito population decline (30 ºC, red dotted line). Right: Average weekly I_M (boxplot, dots = outliers > 2*SD), minimum daily ATMP (red line), and temperature threshold for viral amplification (14.3 ºC, black dashed line) (Reisen et al., 2006).

Spatial forecast

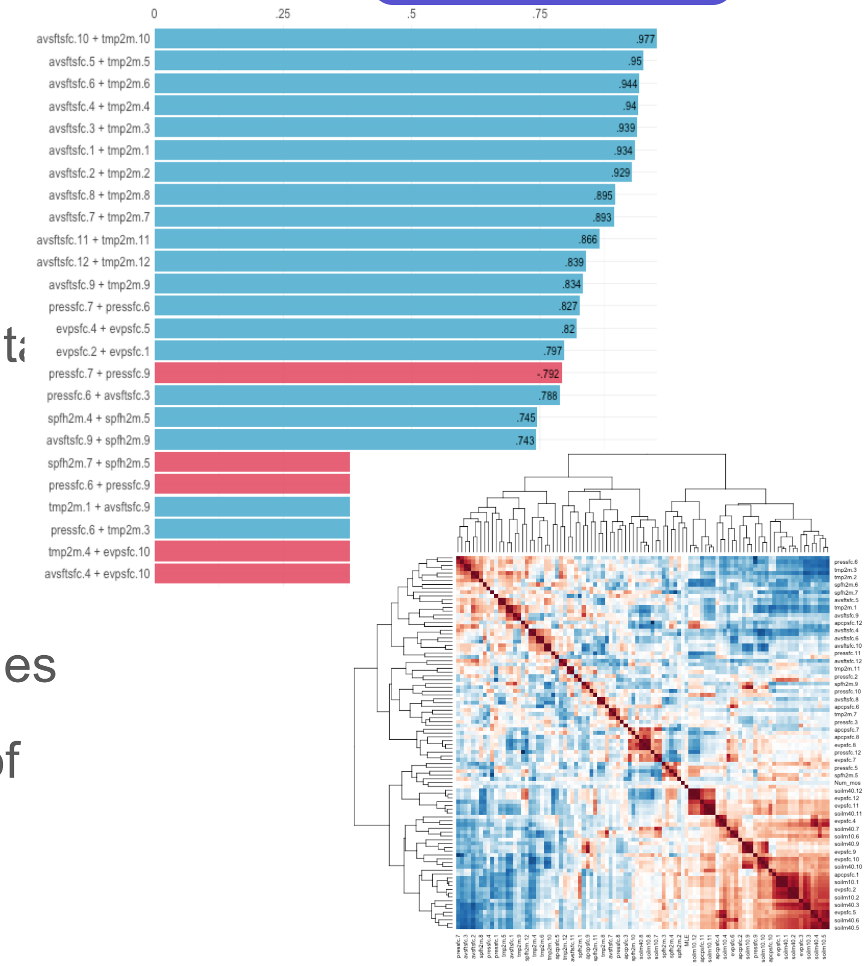
Annual infected mosquitoes



Database Assembly

Spatial forecast

- Downloaded, processed and assembled environmental remote sensing data
- We matched and processed 17 years of mosquito and WNV data to the environmental data
- Evaluated different spatial scales of each environmental data sources
- NLDAS
- Correlation analysis of environmental variables led us to choose a single measure of temperature (ATMP) and a single measure of hydrology (ET) for use in our models
- Nov^{-1} though July to predict annual I_M



Spatial forecast

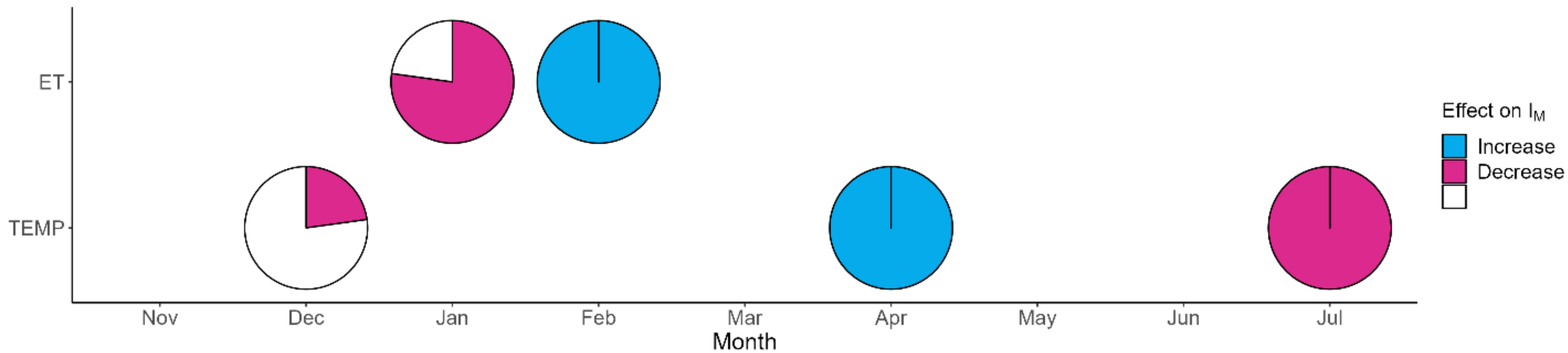
Multi-model inference system

- Annual MLE per 1000 mosquitoes at the NLDAS level as the outcome
- Identified the best models using whole model goodness-of-fit estimated from AIC (Burnham & Anderson, 2002)
- A mixed effects negative binomial model with grid cell as the random effect produced the best AIC
- Used to make predictions with four monthly-environmental variables of ATMP and ET in each model
- Weighted and ranked models selecting the top models whose AIC weights summed to ≥ 0.95
- glmmADMB package in R

Results

Spatial forecast

Environmental predictions at 13 km^2



Cooler/drier winter

- Birds migrating into valley
- Mosquitoes and birds in same location - Salton Sea ("Island Effect")
- WNV

Warm/wetter spring

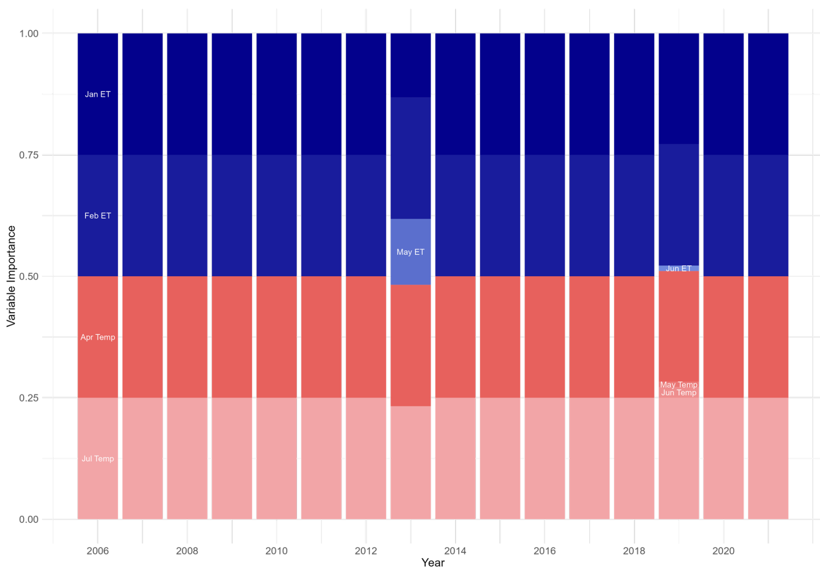
- Shortened EIP
- Faster mosquito reproduction and development
- Continued Island Effect

Cooler summer

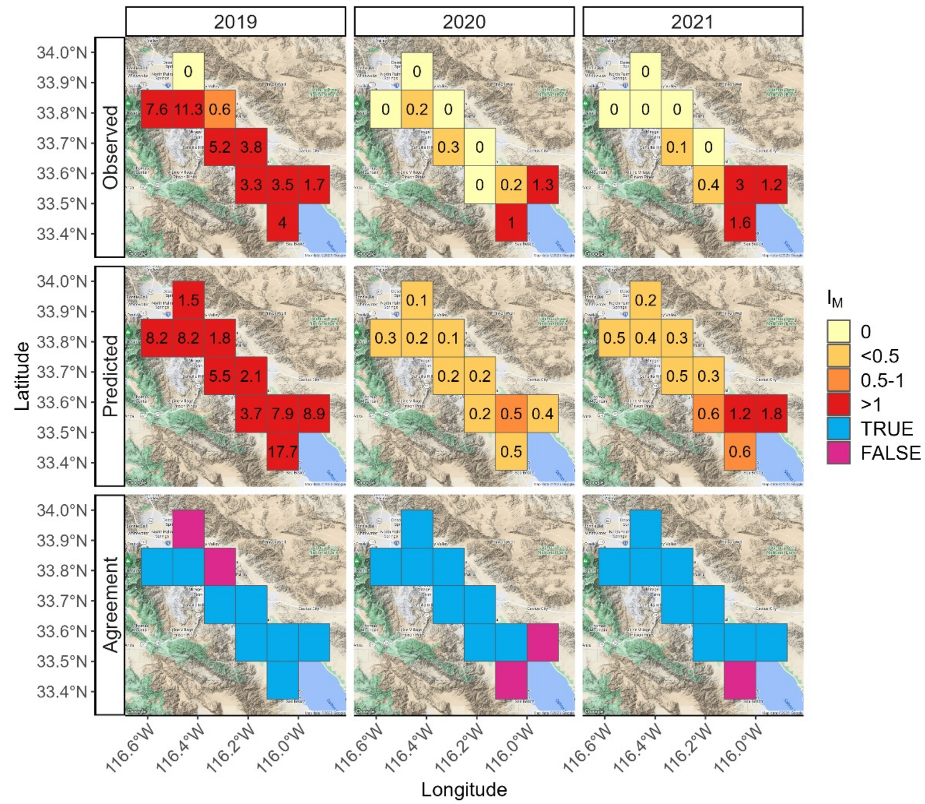
- Transmission continues
- High heat events characteristic of CV summers postponed
- WNV able to spread North

Validation

- LOYO; 2006 - 2018
- 2006 - 2018 -> predicted 2019, 2020, 2021
- compared observed vs. predicted
- 2006 - 2021 -> predict 2022



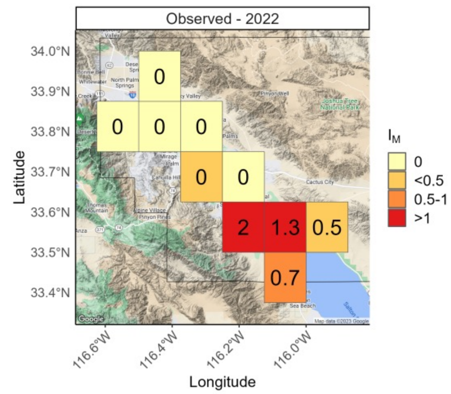
Variable weights contributing to LOYO models for 2006 - 2021 (Red = ATMP, Blue = ET). Year indicated the annual data removed from the LOYO model.

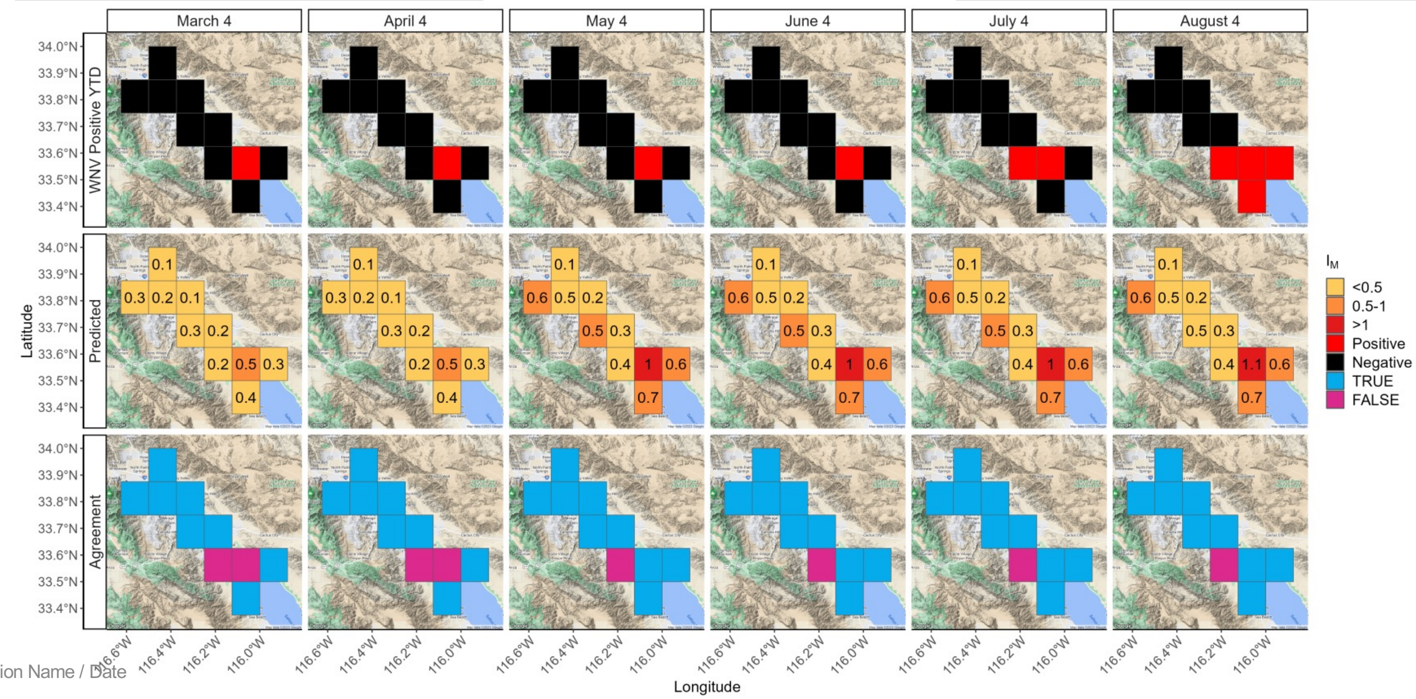


Agreement between observed and predicted I_M stratified by NLDAS grid in the CV for 2019 - 2021. Top Row: Observed I_M in 2019, 2020, and 2021. Middle Row: Predicted I_M in 2019, 2020 and 2021 using a four-predictor model ensemble trained on years 2006 - 2018. Bottom Row: Proportion of cells in agreement with the ensemble model using one infected mosquito per 1,000 tested as a cutoff value/threshold.

Real-time forecast 2022

Results

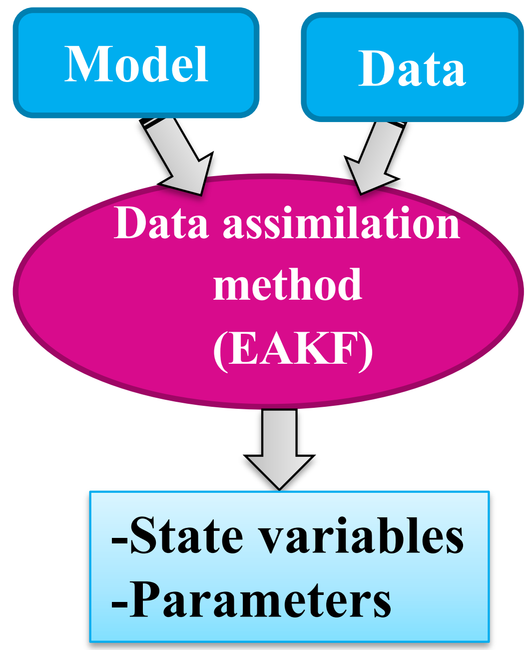




temporal forecast

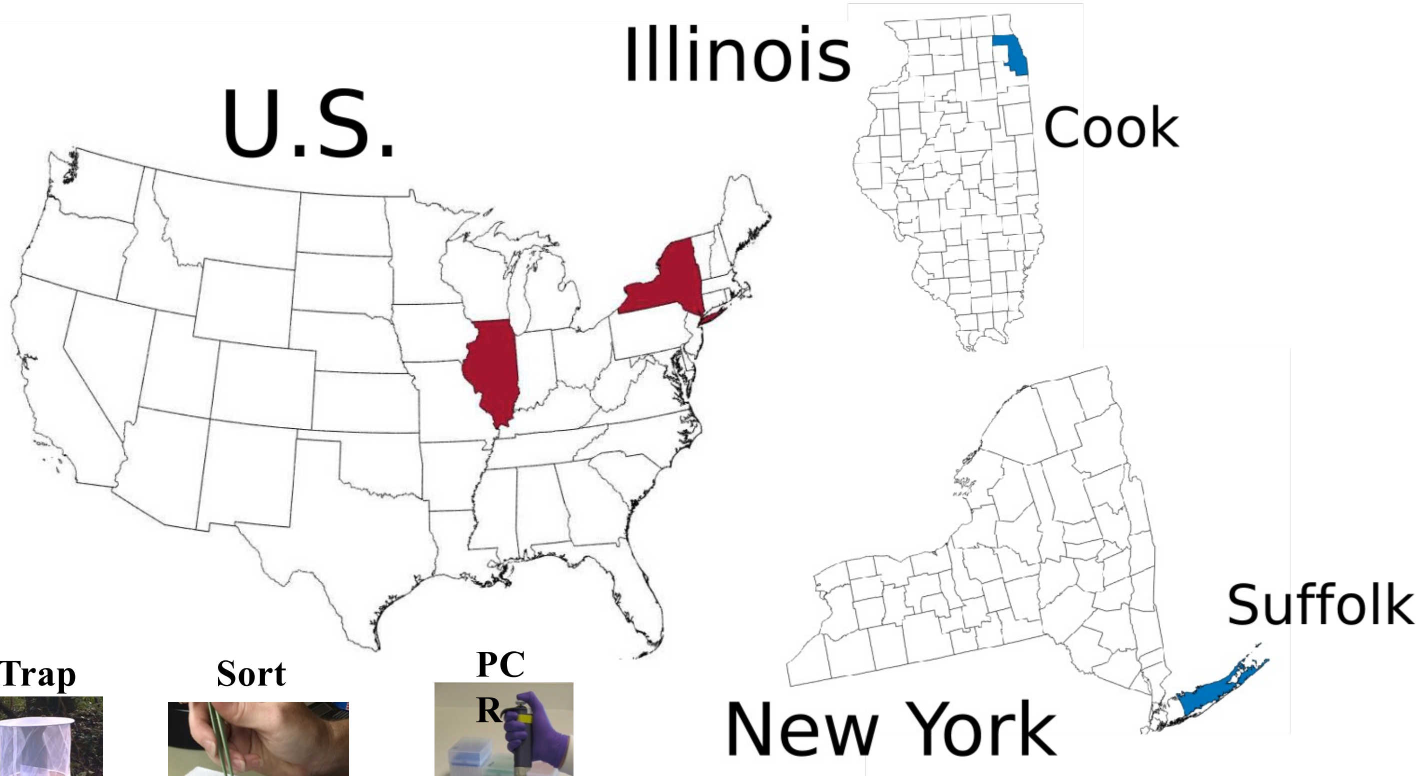
Forecast System

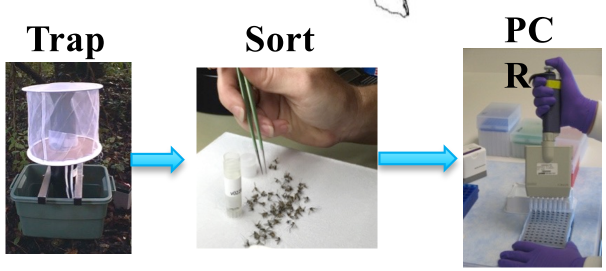
- Model-EAKF system relies on three components:
  1. WNV surveillance data
  2. Mathematical model that can freely simulate the spread of WNV in mosquitoes, birds, and humans
  3. Data assimilation method
     - Ensemble adjustment Kalman filter (EAKF)



Data

Monitoring Data



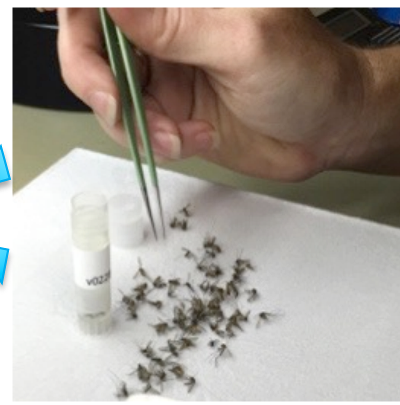


Data

Mosquito Surveillance

Mosquito trap

Mosquito identification



Polymerase chain reaction

Data

Pooled Testing

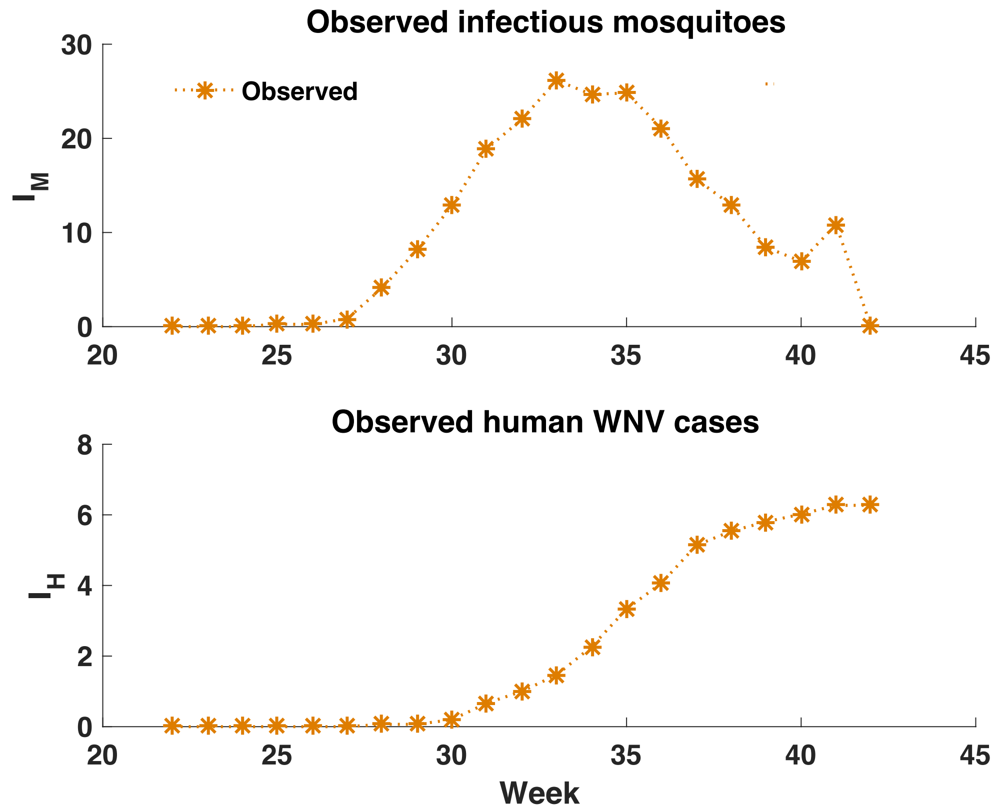
Maximum likelihood estimation

- Estimate the proportion of infected mosquitoes in the wider population
- Assume it follows a Bernoulli distribution
- Numerically solve for the minimum due to different samples sizes of mosquitoes

Date	Week Number	No. Mosquitoes	+/-	Trap Location
8/4/14	32	38	0	1
8/4/14	32	42	1	2
8/7/14	32	47	0	3
8/7/14	32	50	0	3
8/7/14	32	50	0	3
8/11/14	32	23	0	4
8/12/14	32	36	1	5
8/12/14	32	42	1	6
8/13/14	32	45	0	7

Data

Average Outbreak Structure

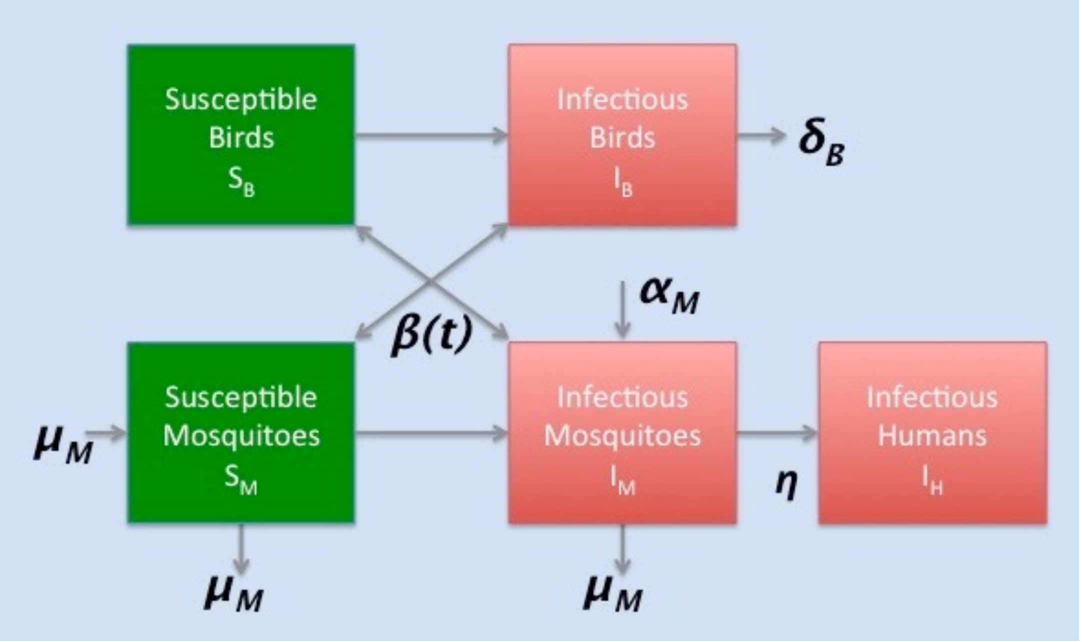


Model

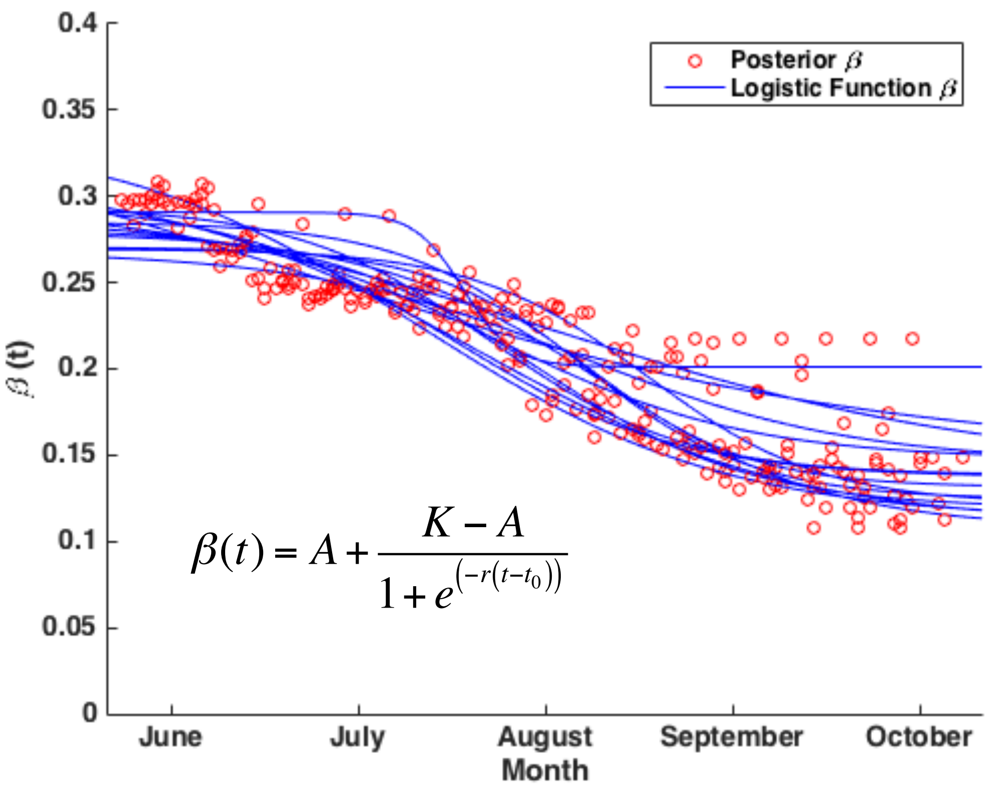
Baseline Compartmental Model

Parameters:

- μ_M– birth and death rate of mosquitoes
- δ_B– bird recovery rate
- $\beta(t)$ – contact rate between birds and mosquitoes at time t
- η –risk of spill-over to humans

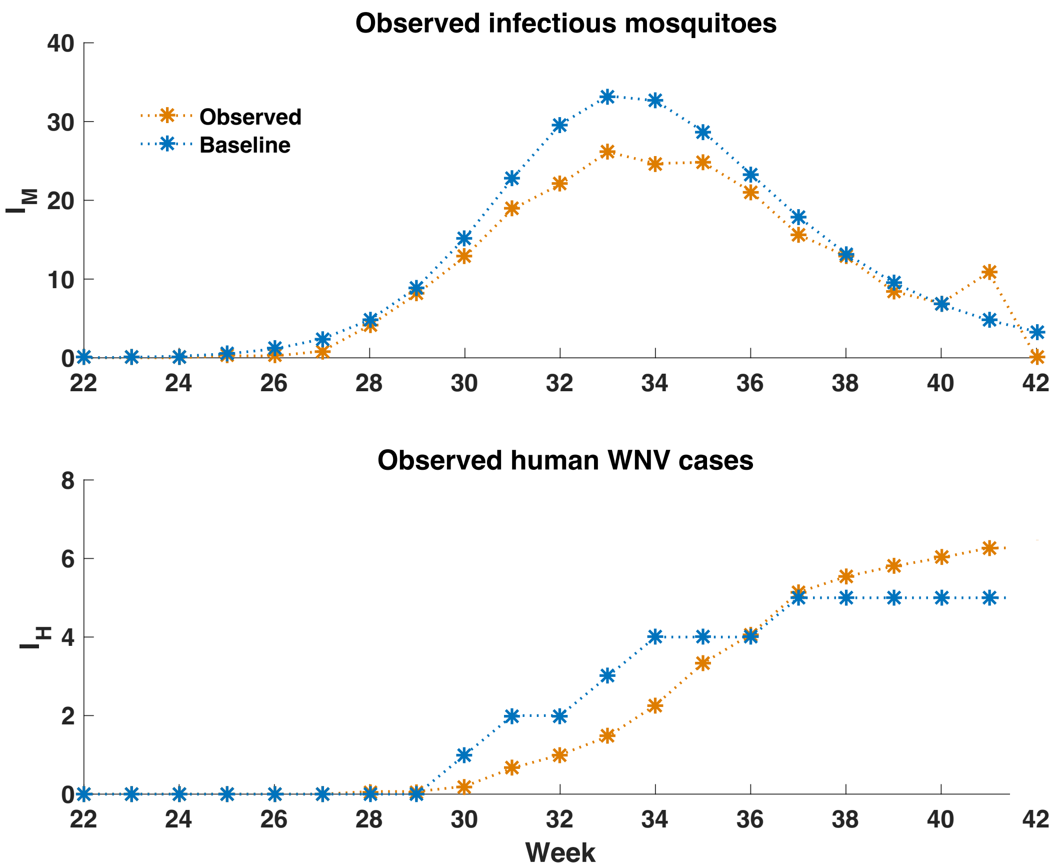


Mosquitoes feeding patterns,
Impact transmission between birds and mosquitoes



Model

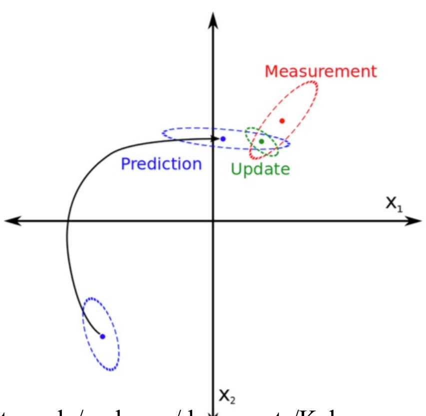
Simulation of Outbreak



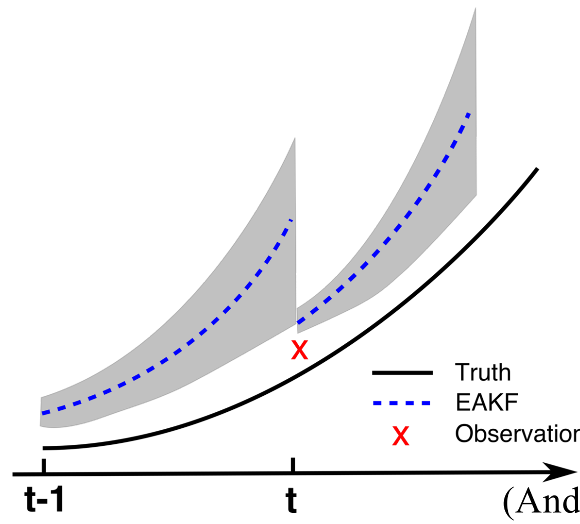
Filtering method (EAKF)

Ensemble Adjusted Kalman Filter

- Data assimilation technique designed to estimate the true state of a system given both observations and model simulation of that state
- Unobserved state variables and parameters are adjusted using cross ensemble co-variability



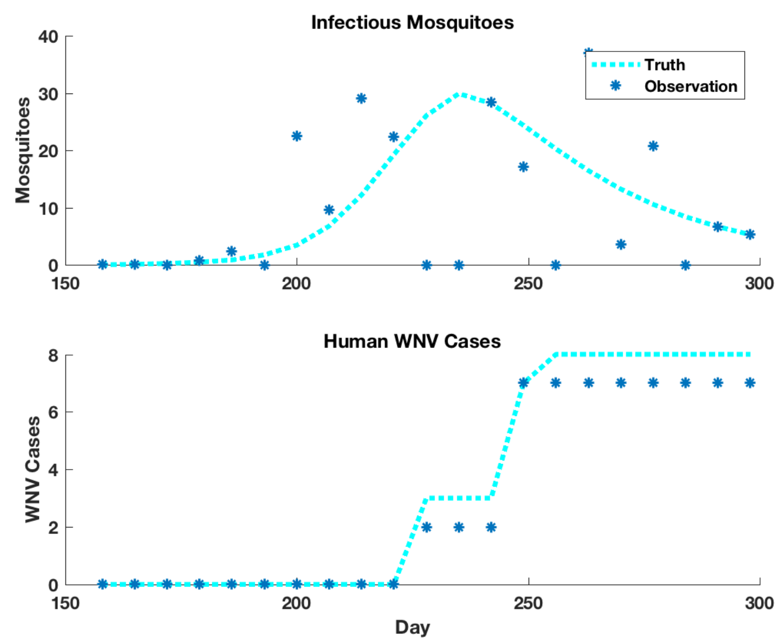
http://www.princeton.edu/~adamsc/documents/KalmanFilterBayesDerivation.pdf



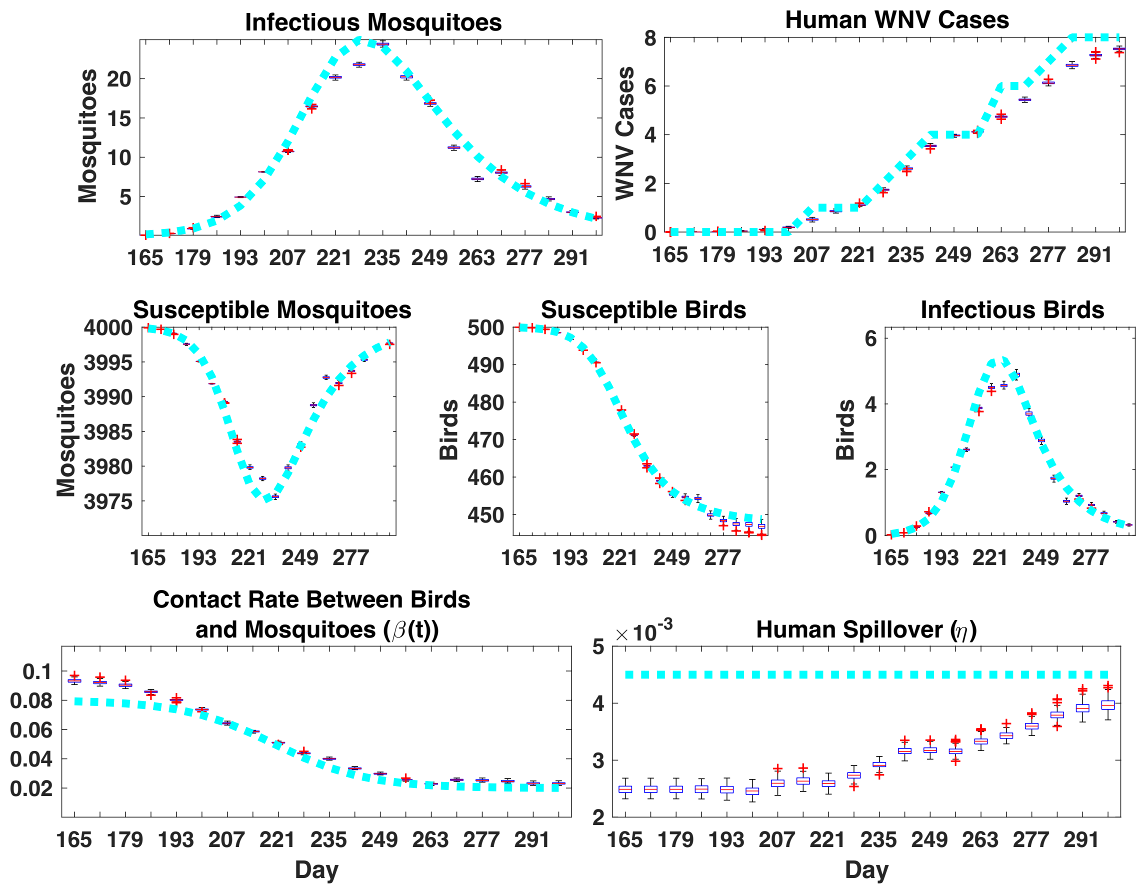
(Anderson 2001)

EAKF Optimization

- 12 dimensional system
- Can the EAKF optimize this?
  - Given 2 data streams
- In real world do not know the truth
- Model simulation we know state variables and parameters

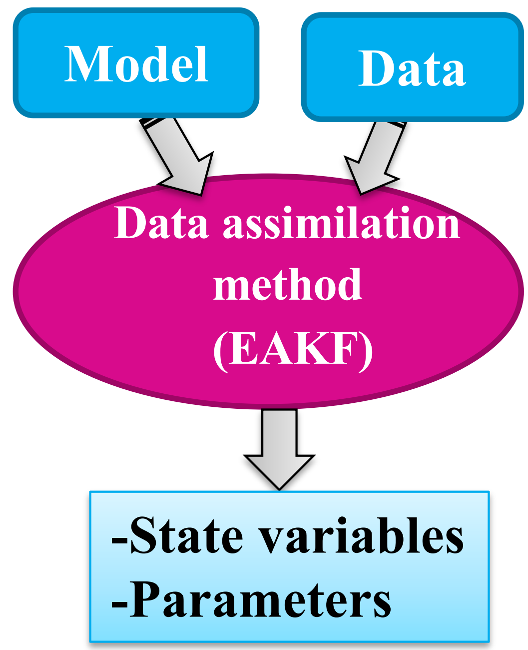


Synthetic Test



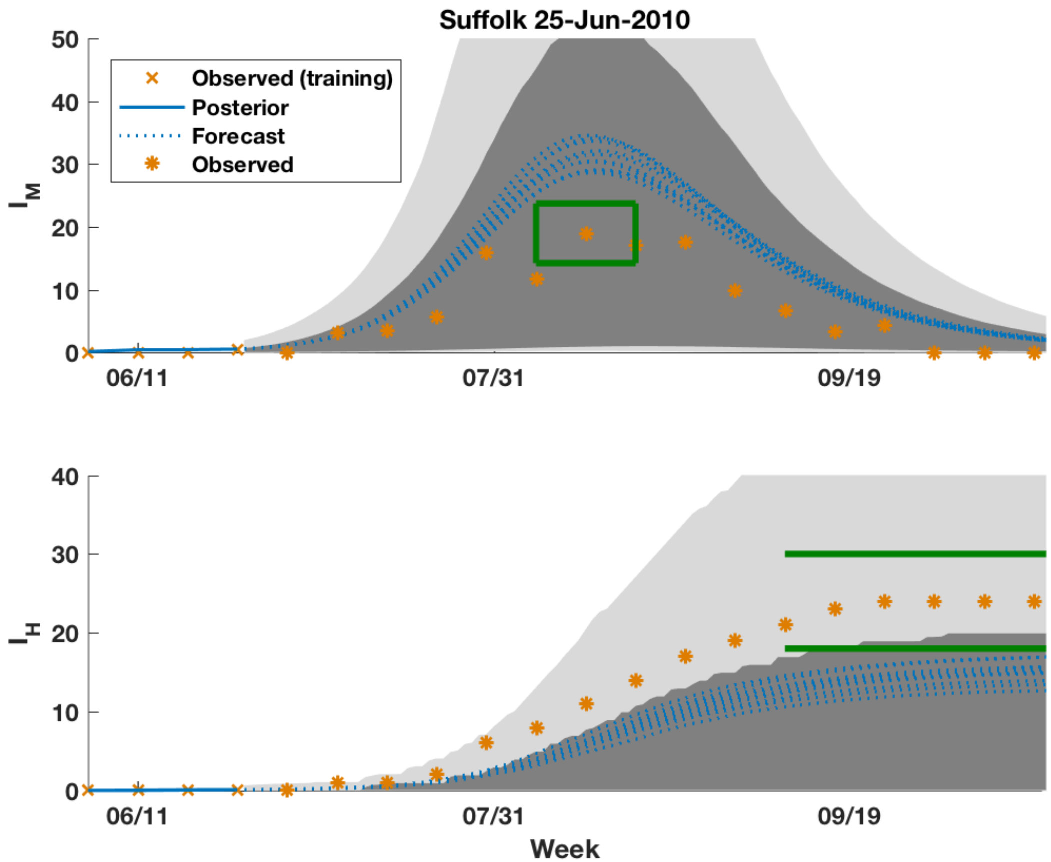
Forecast

- Training period:
  - Model-EAKF system updates state variables and parameters
  - Updated model is better aligned with local dynamics of the observed outbreak
- Forecast:
  - Simulate model to end of season



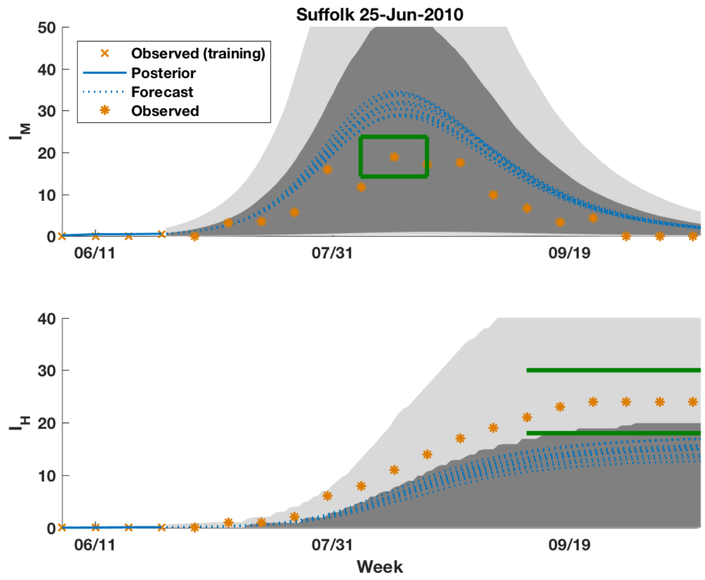
Results

Retrospective Forecast



Results

Forecast Accuracy

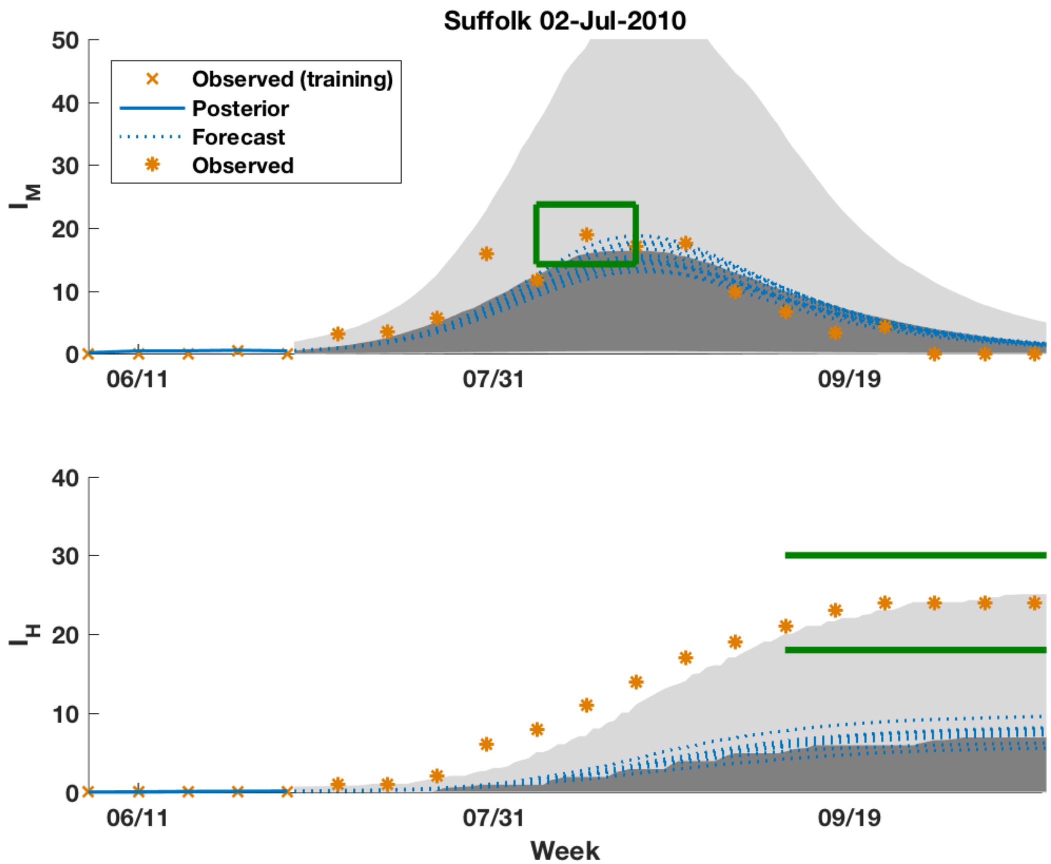


A forecast was deemed accurate if:

- ± 25% total number of human cases
- Peak timing within ± 1 week of the observed peak of infectious mosquitoes
- Maximum mosquito infection rate was within ± 25% of the observed peak infection rate

Results

Retrospective Forecast



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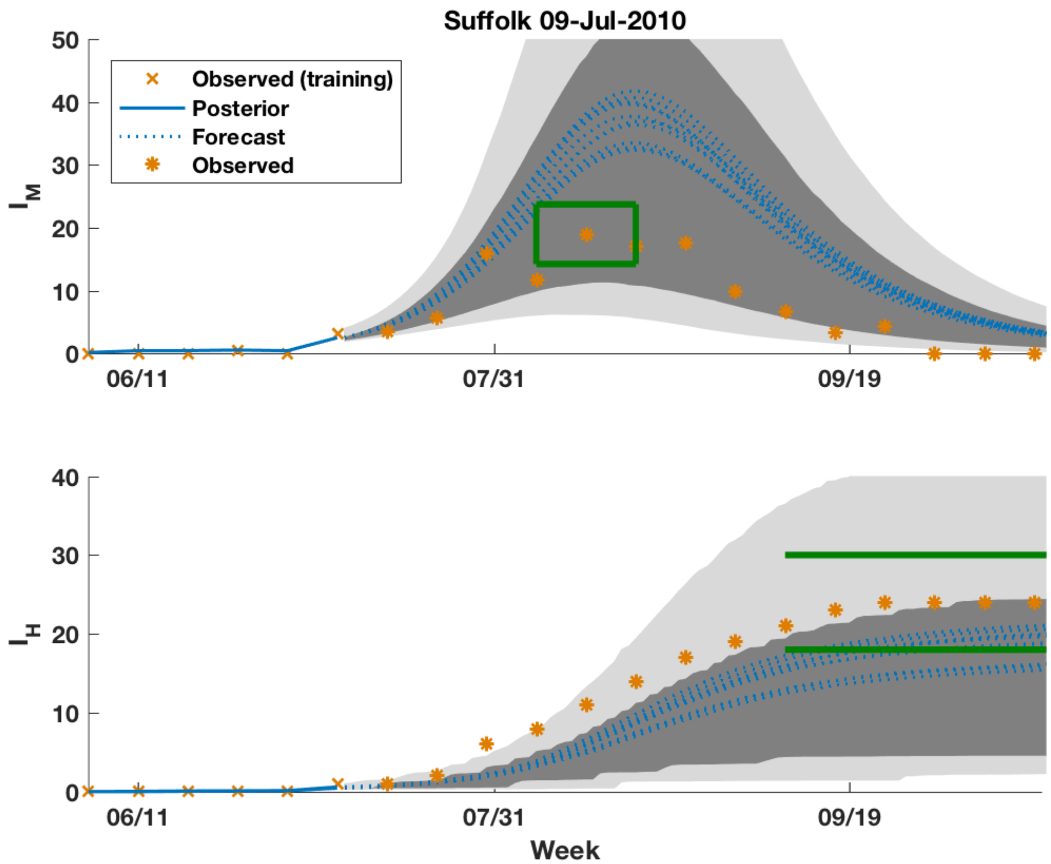
Retrospective Forecast



Results

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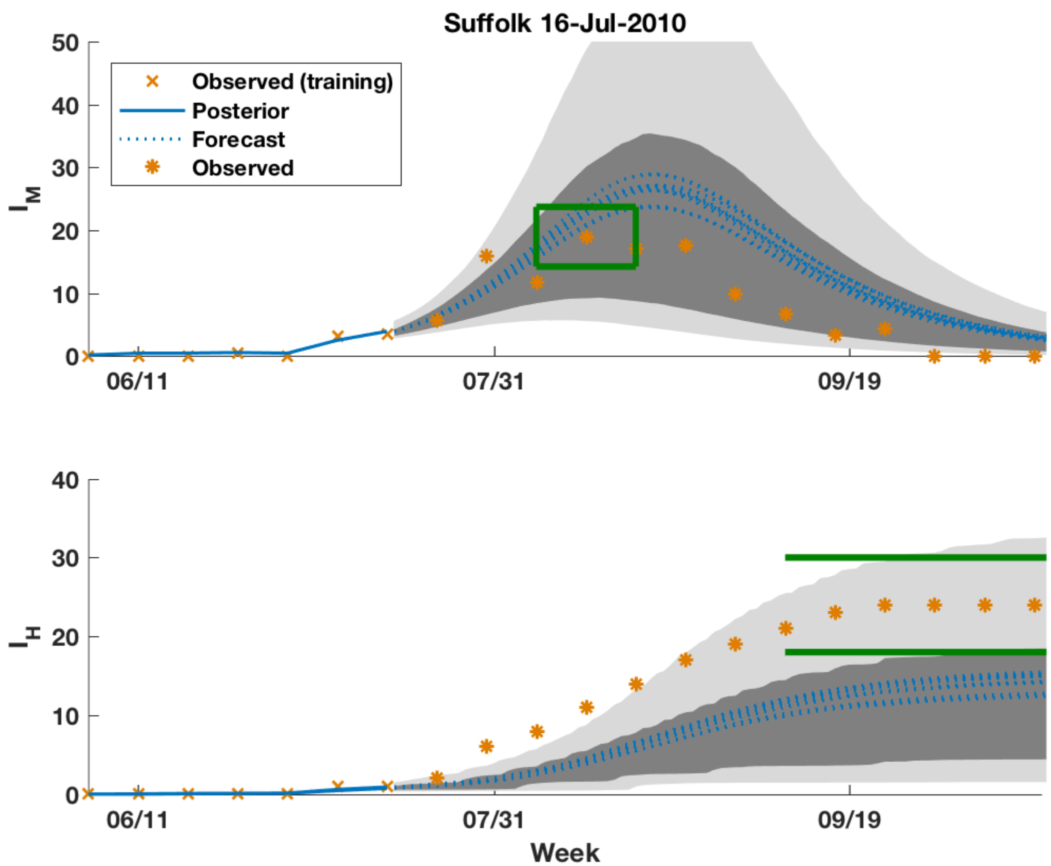
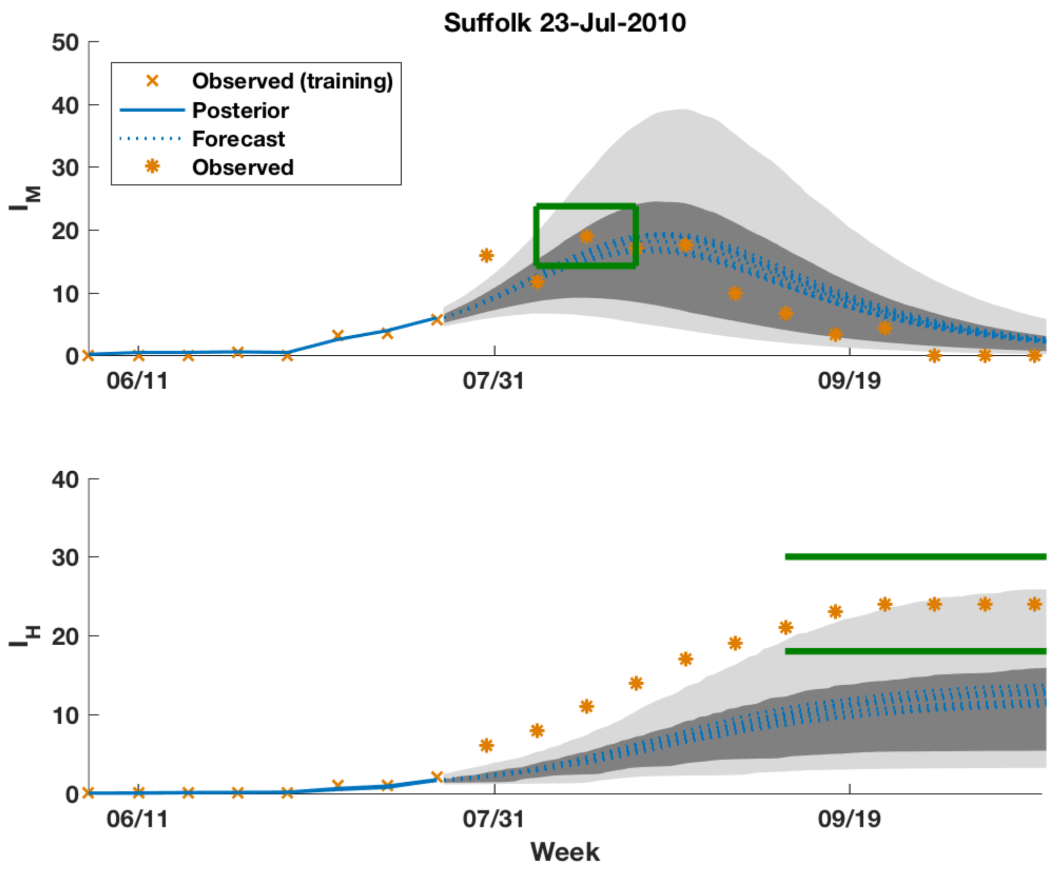


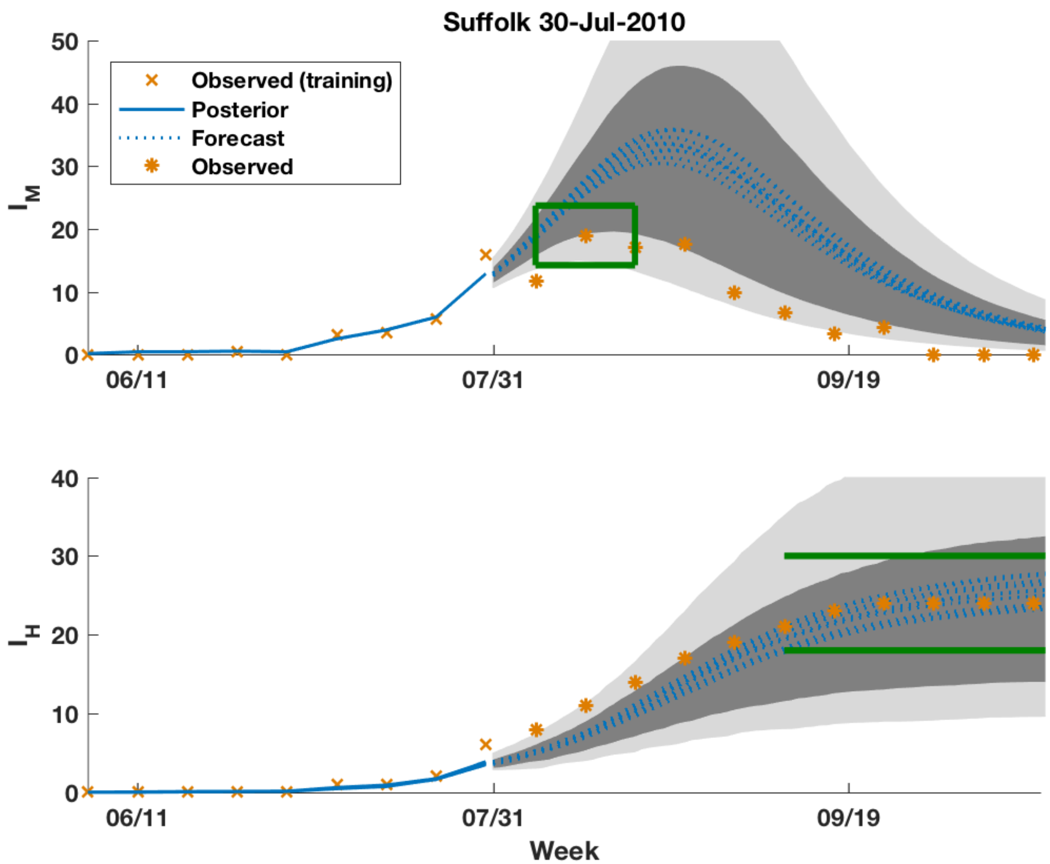
Results

Retrospective Forecast



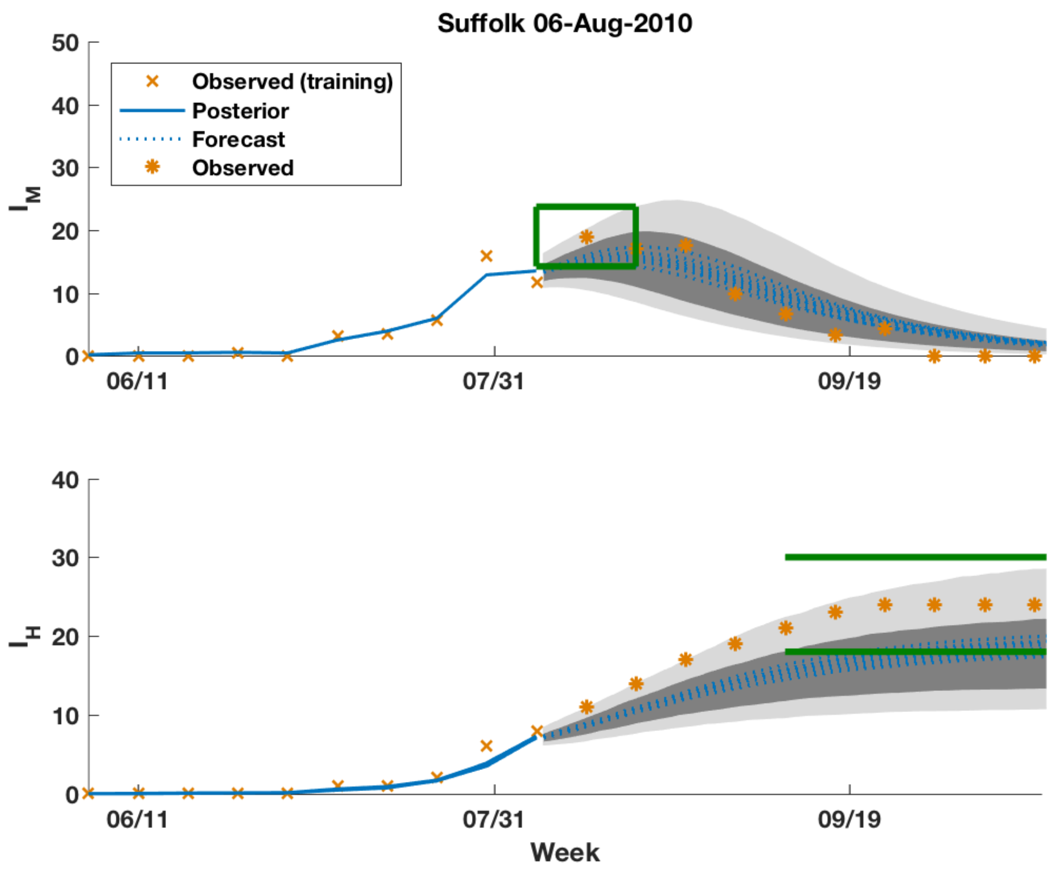
Results

Retrospective Forecast



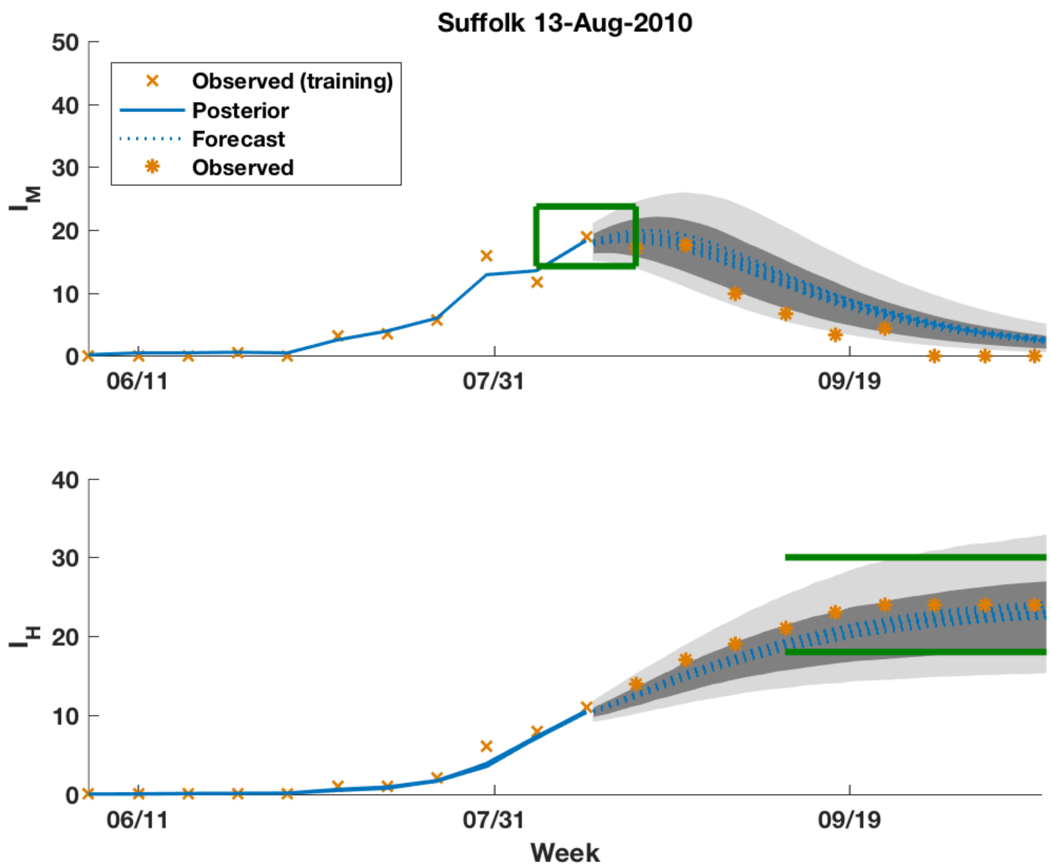
Results

Retrospective Forecast



Results

Retrospective Forecast



Results

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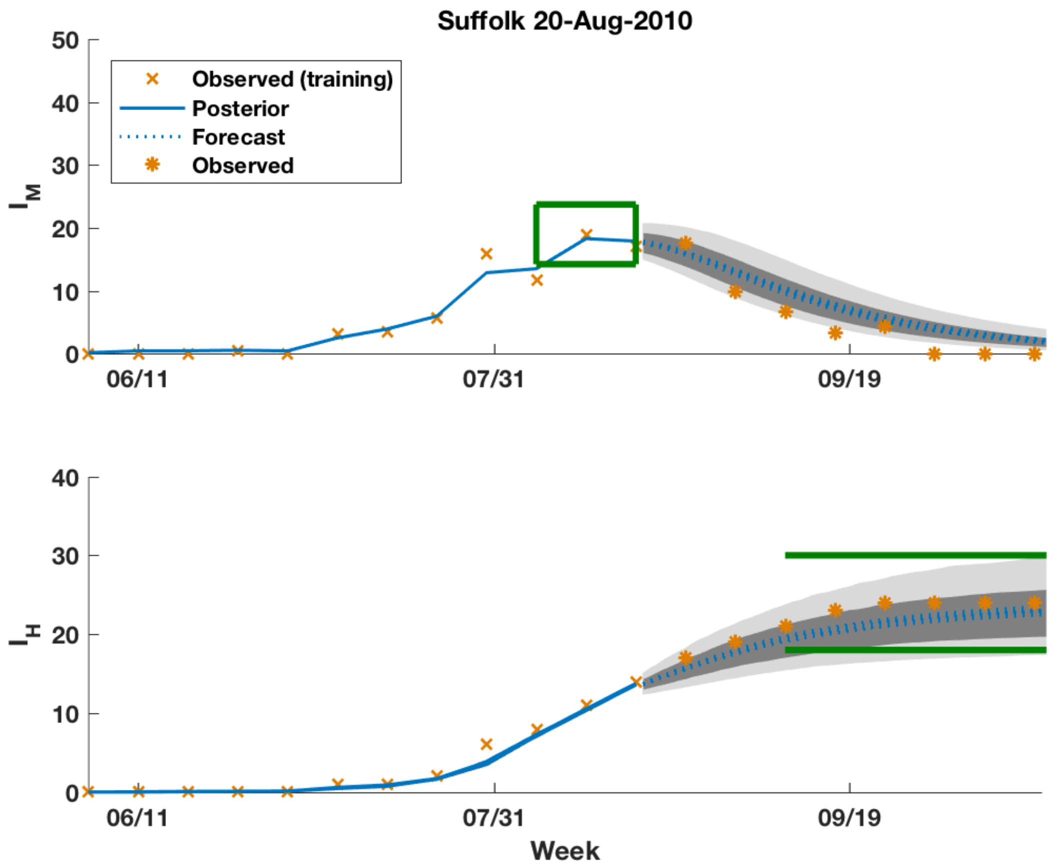

Results

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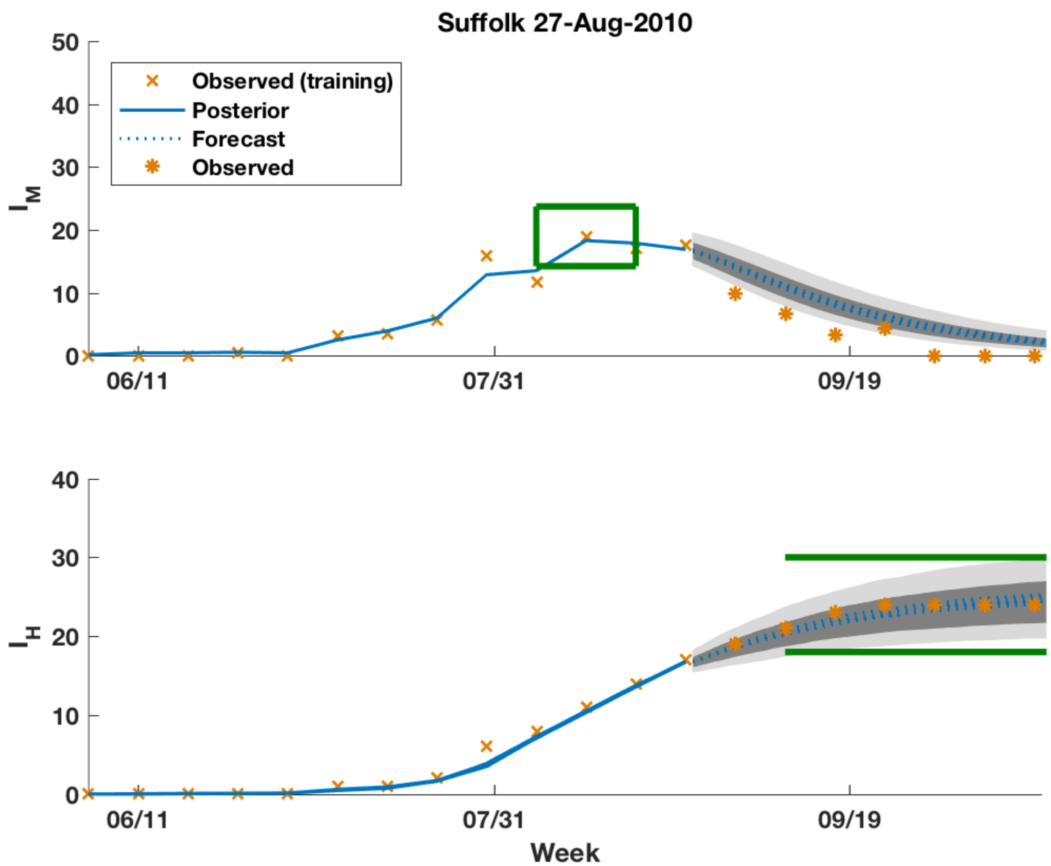

Results

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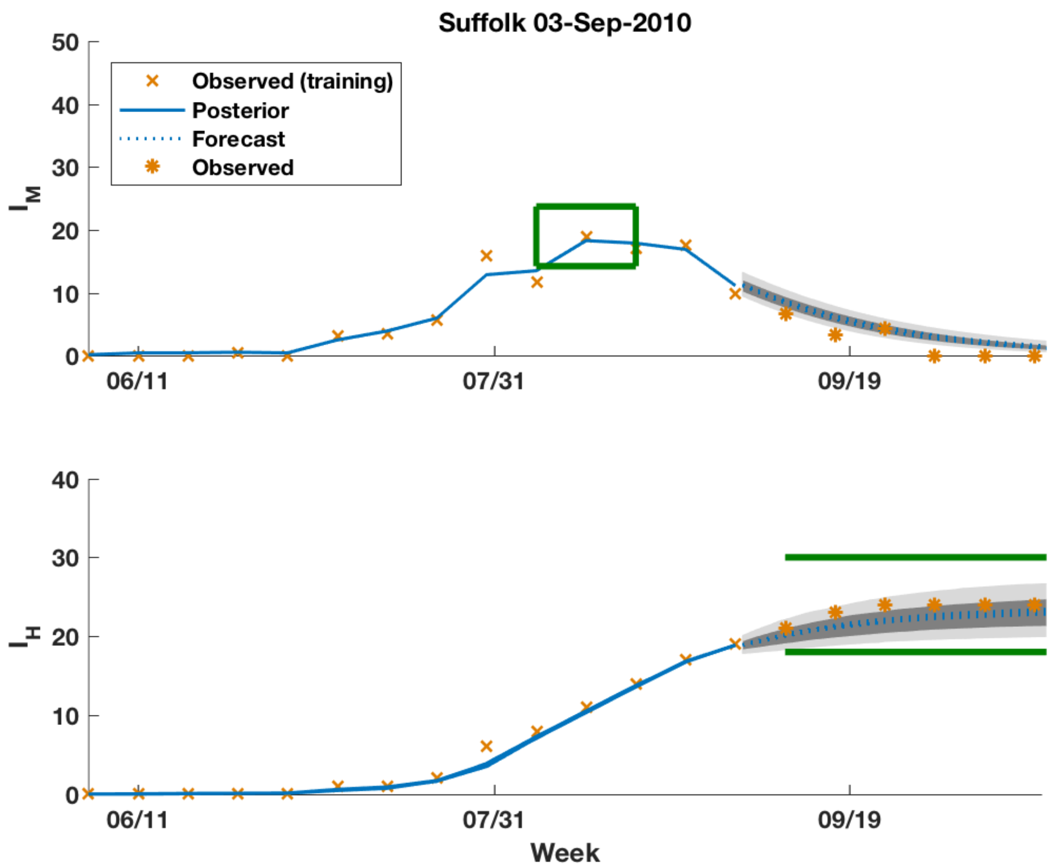
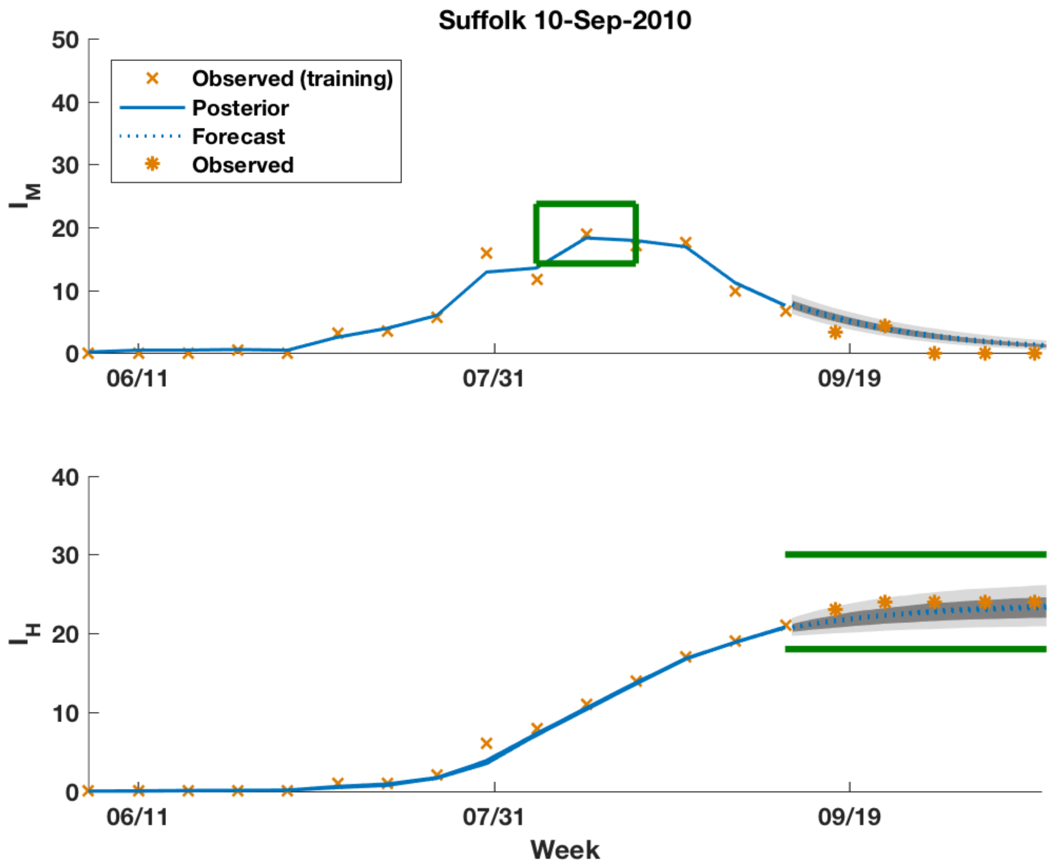


Results

Retrospective Forecast



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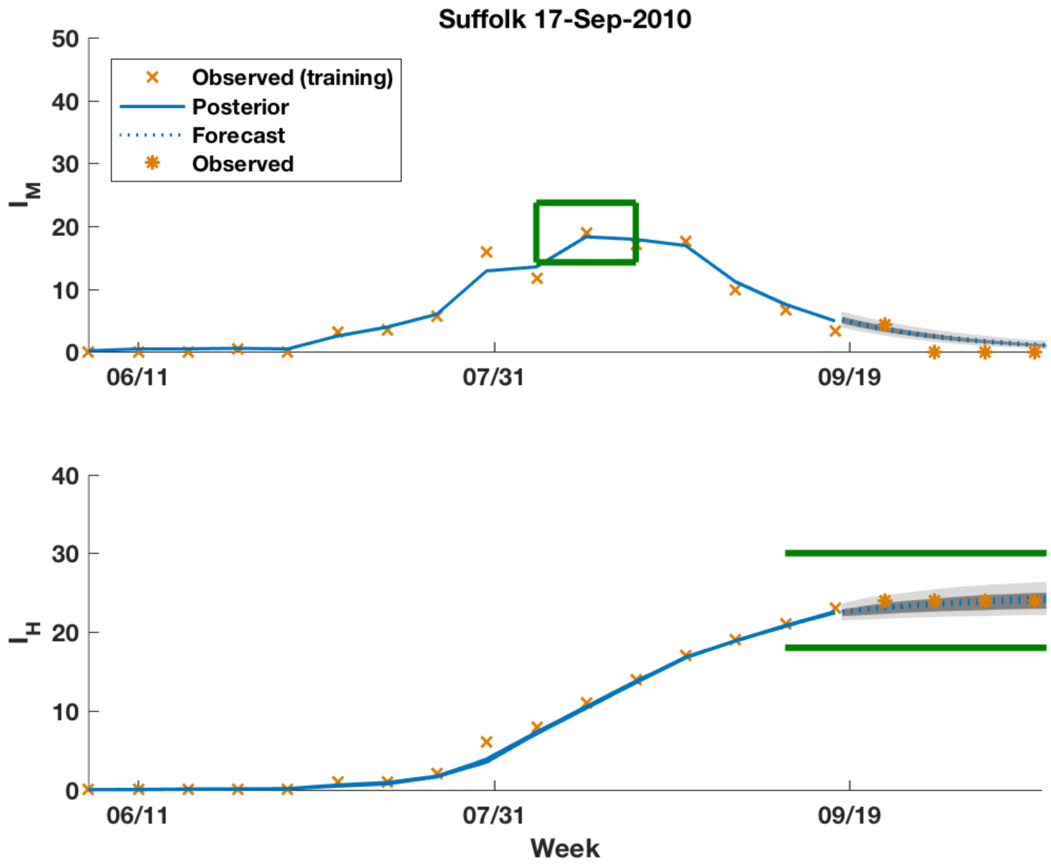

Results

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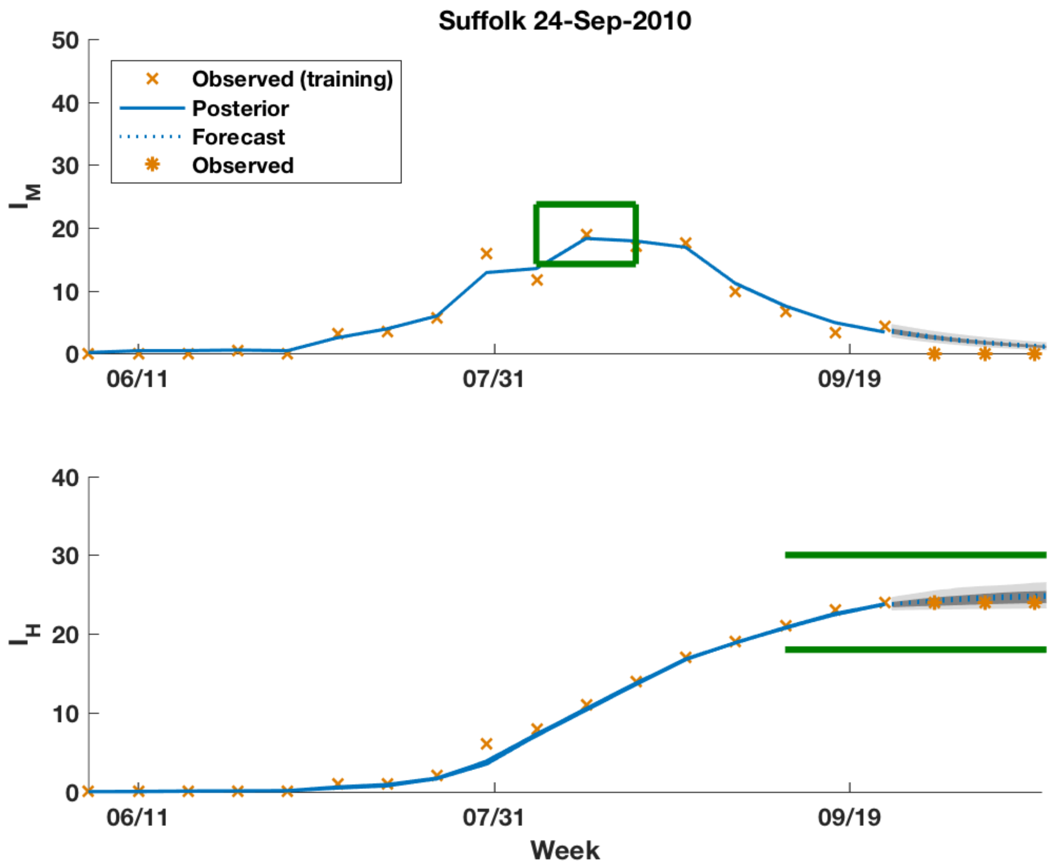

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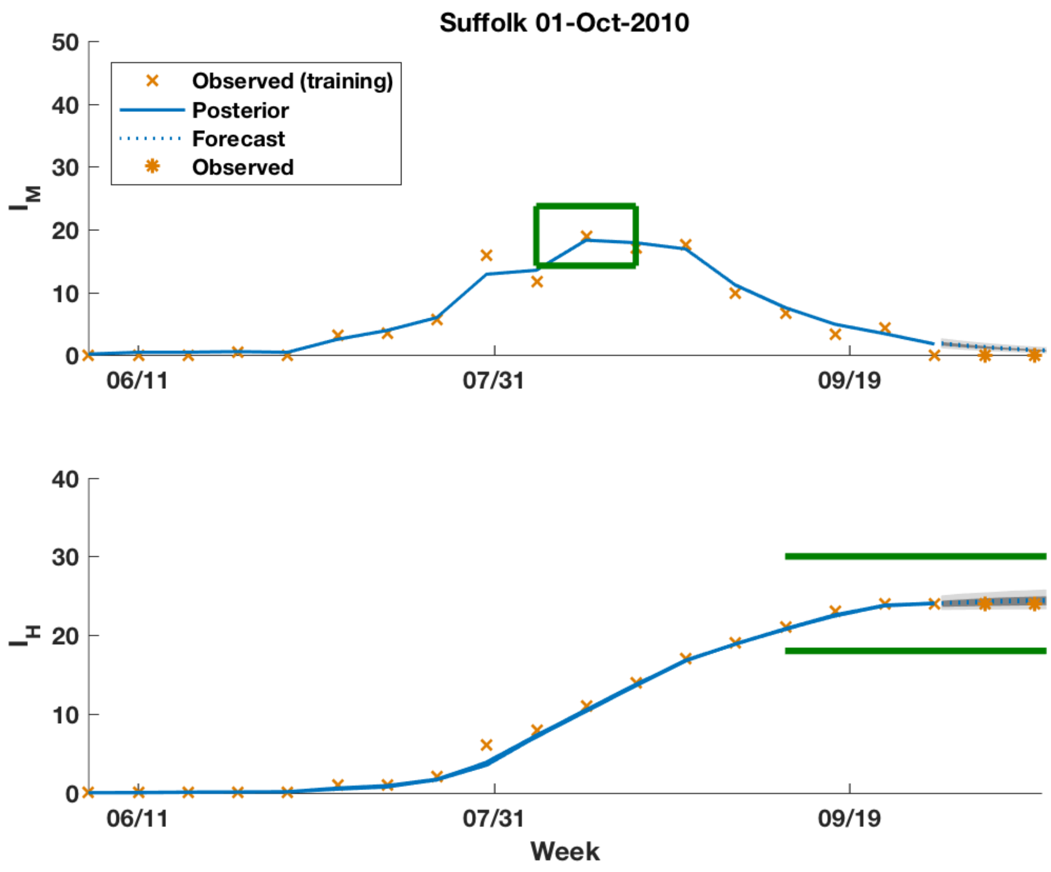

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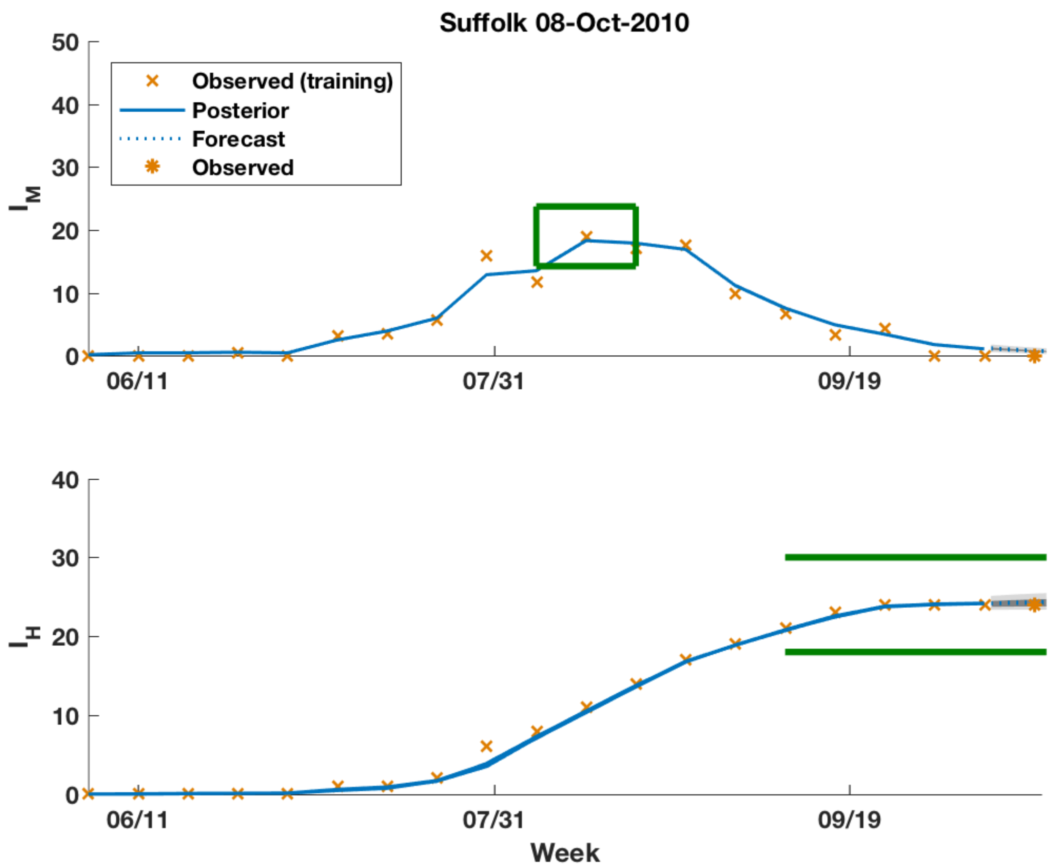
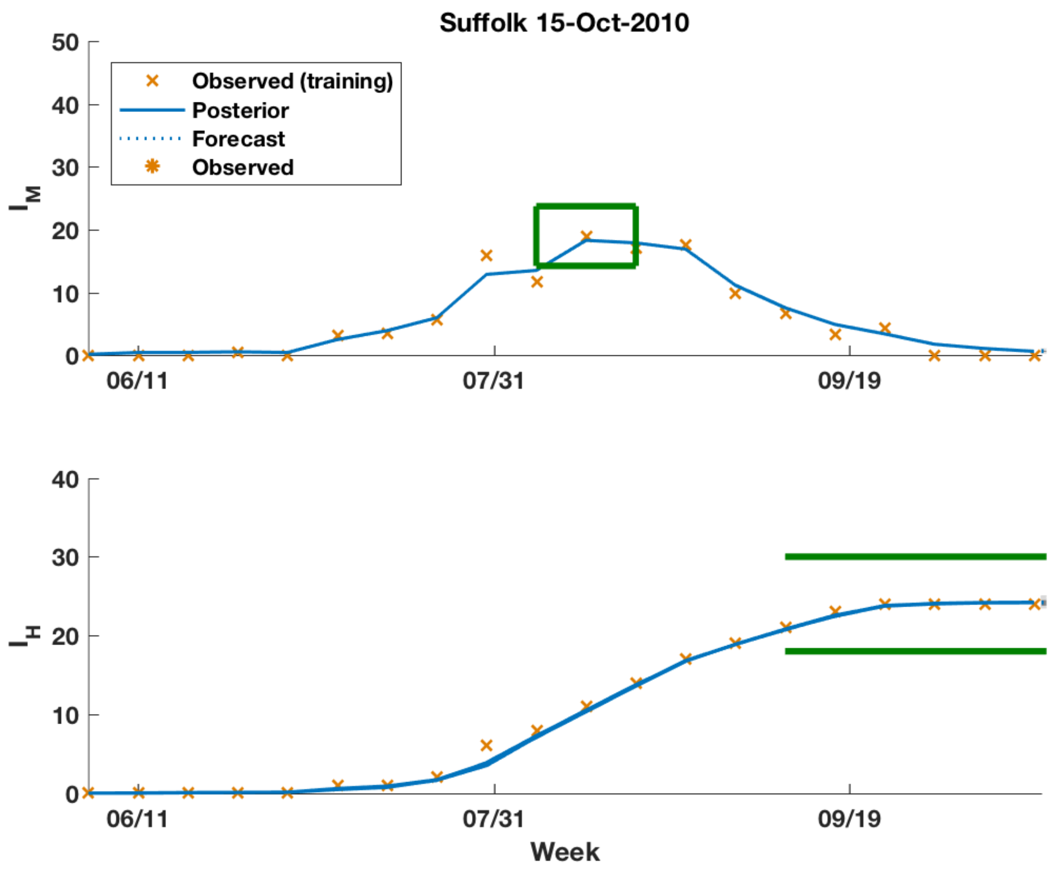
Retrospective Forecast



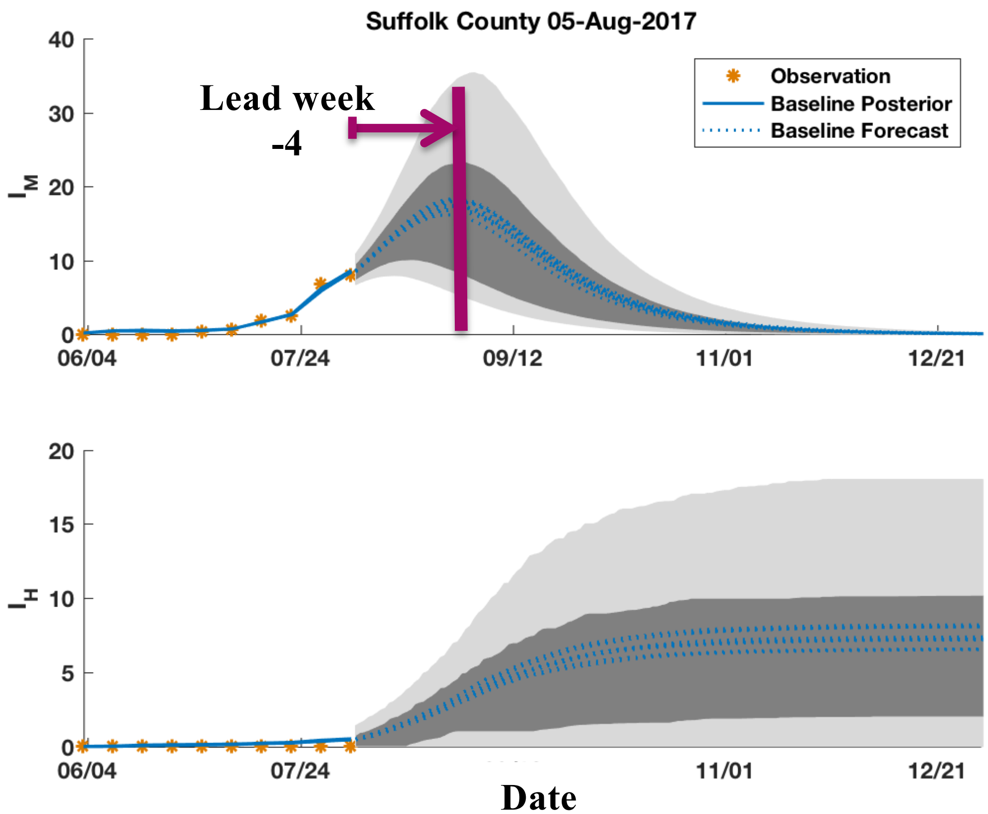
Results

Retrospective Forecast



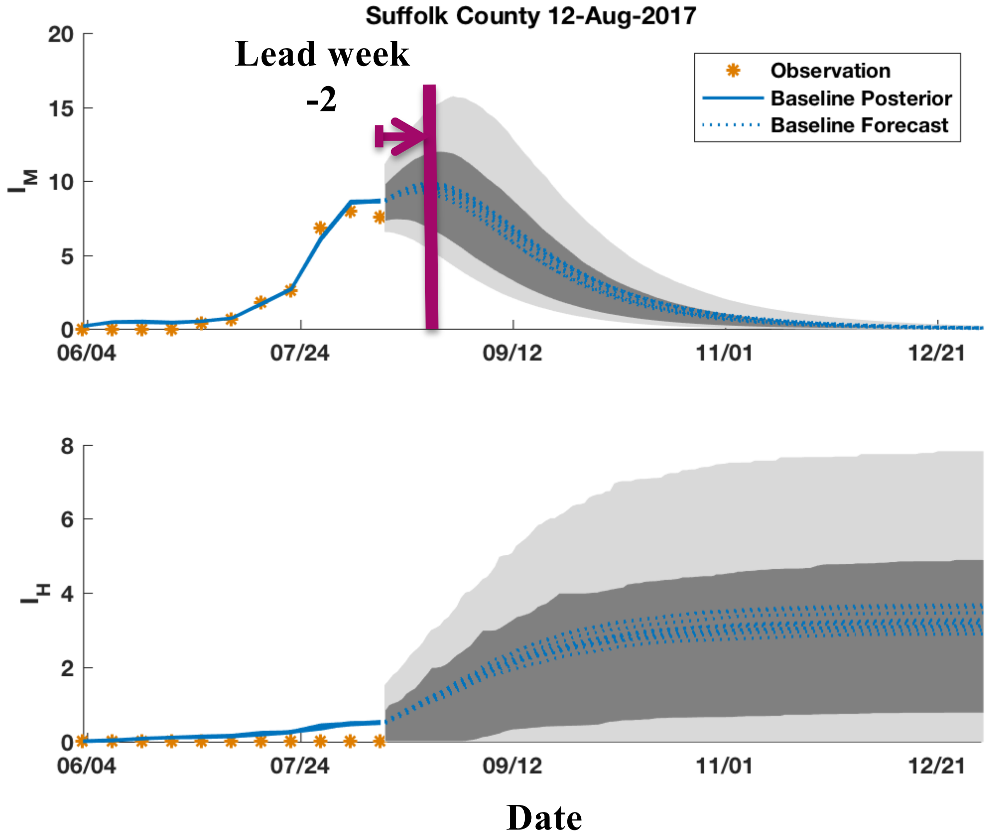
Calibration

Lead Week Explanation



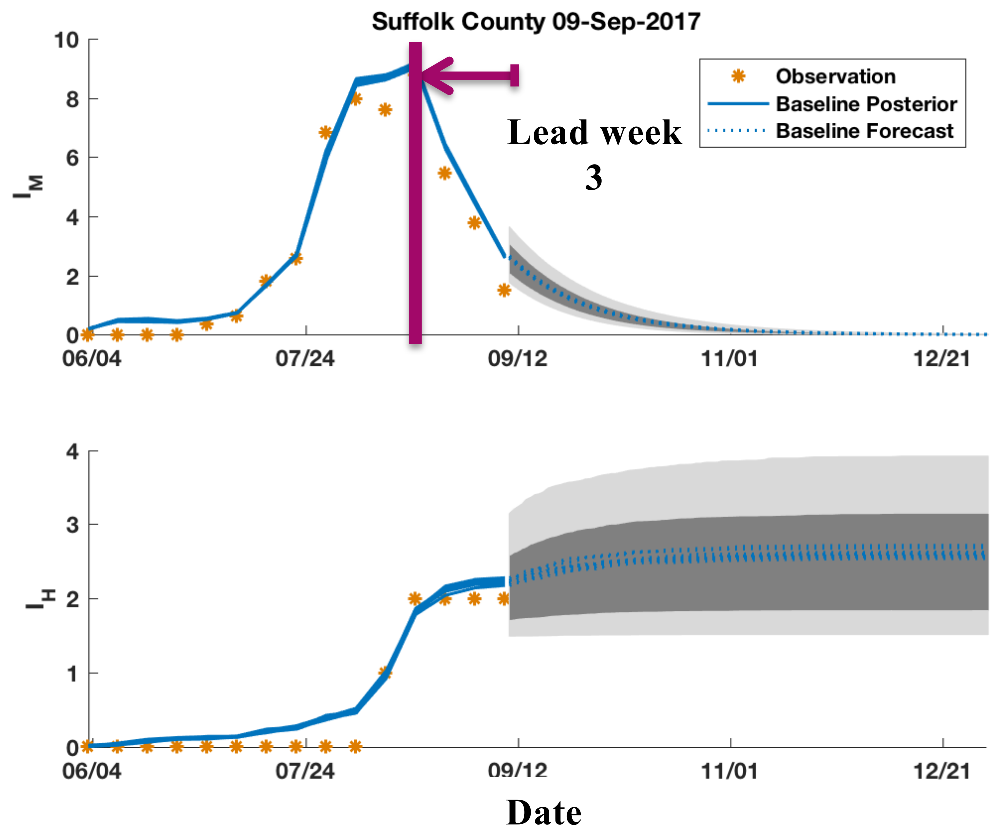
Calibration

Lead Week Explanation



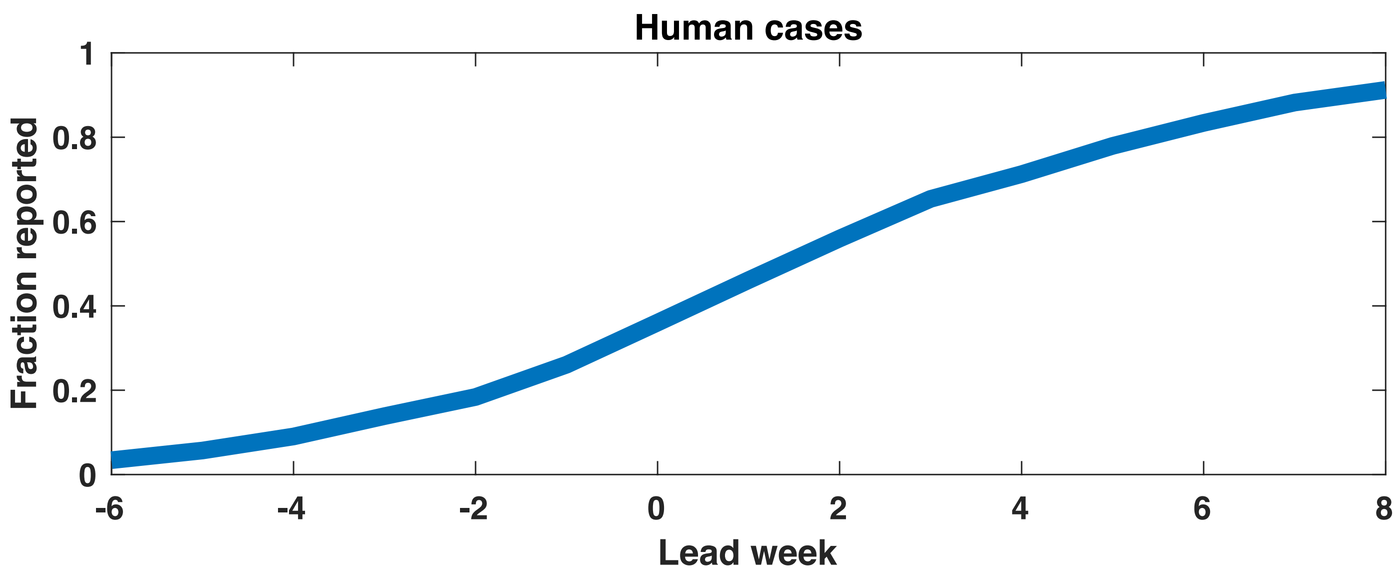
Calibration

Lead Week Explanation

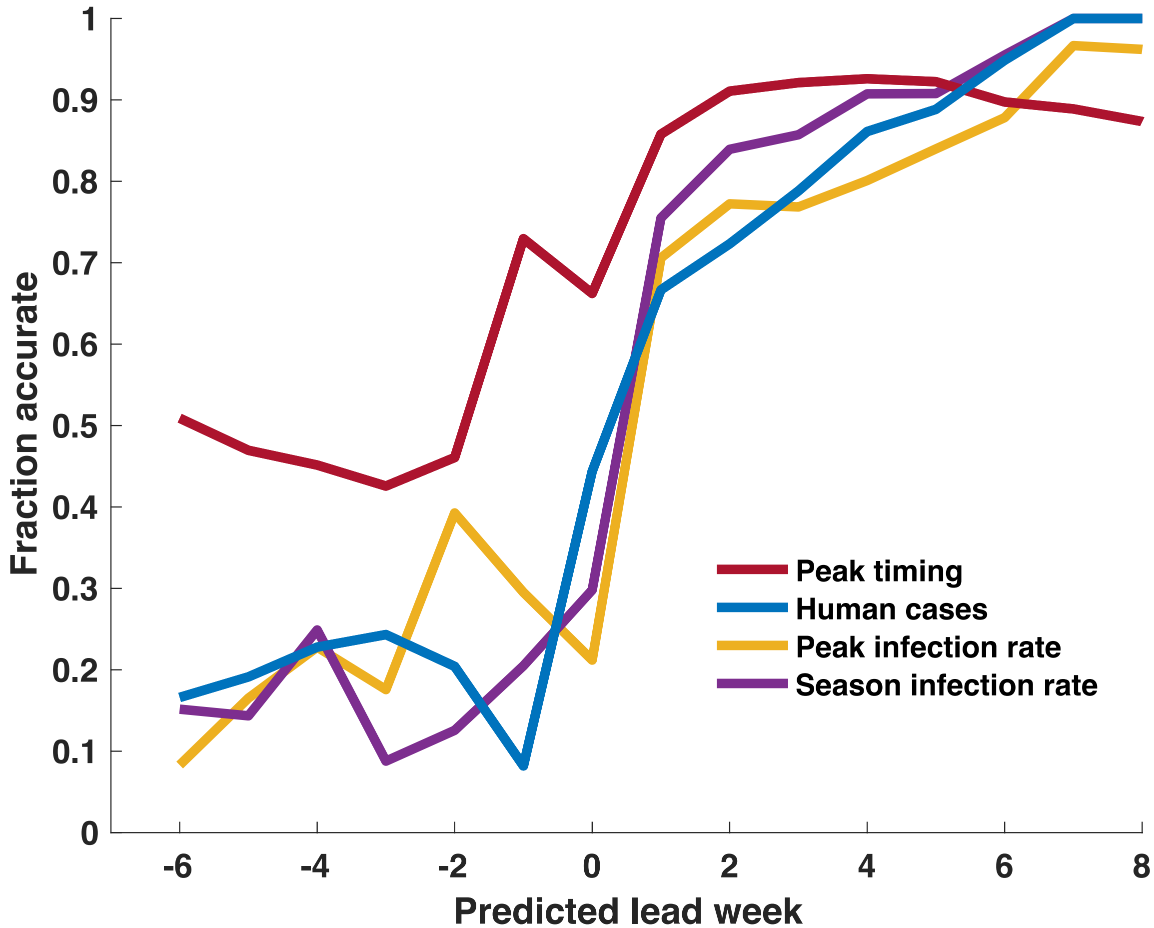


Data

Human Cases Lead Week

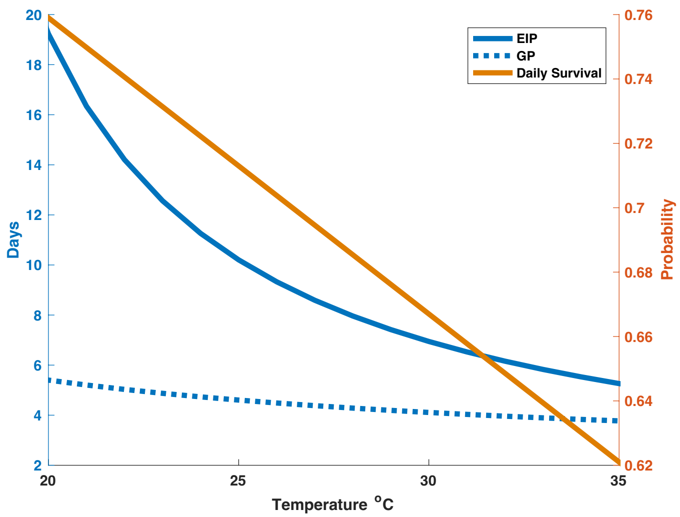


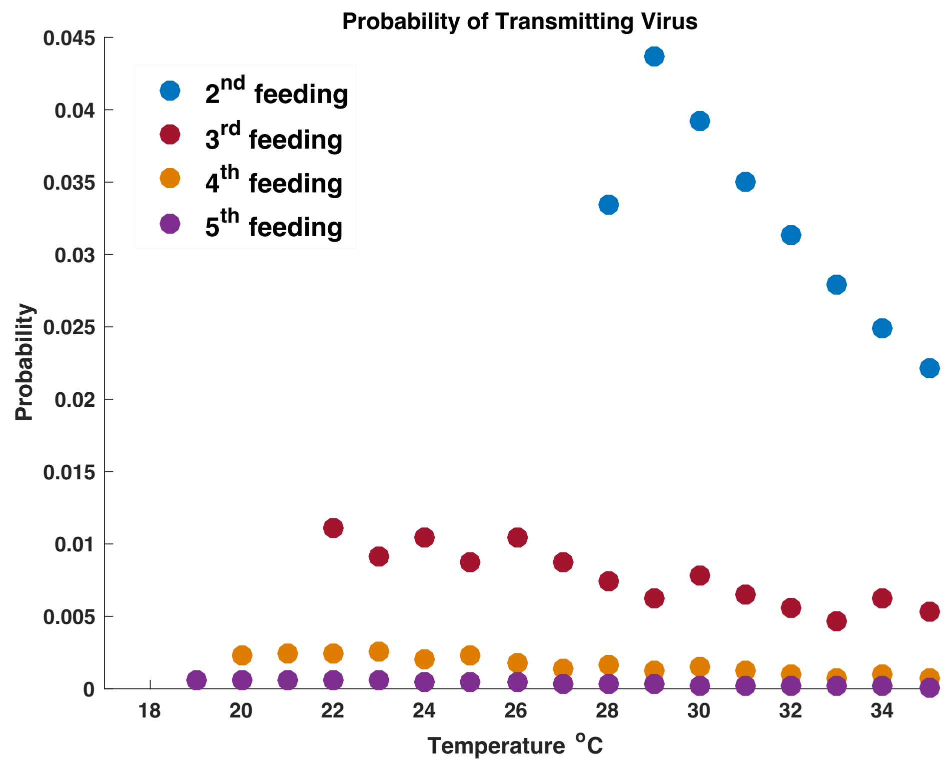
Forecast Calibration



Background

Mosquito Survival to Transmit

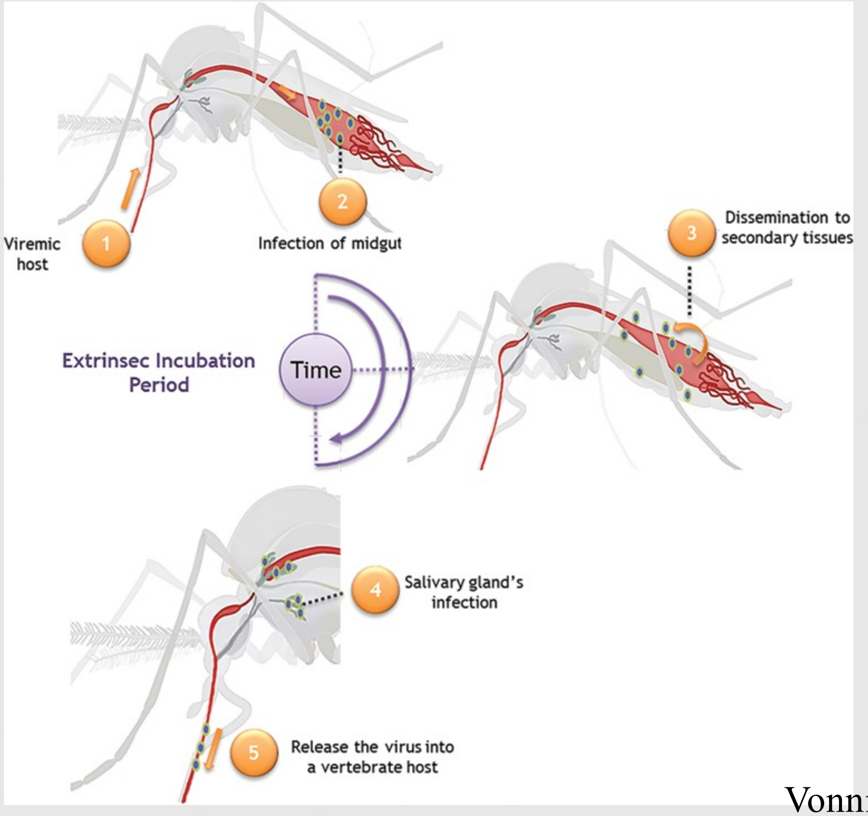




Reisen et al. 1992; Reisen et al. 2006; Hartley et al. 2012

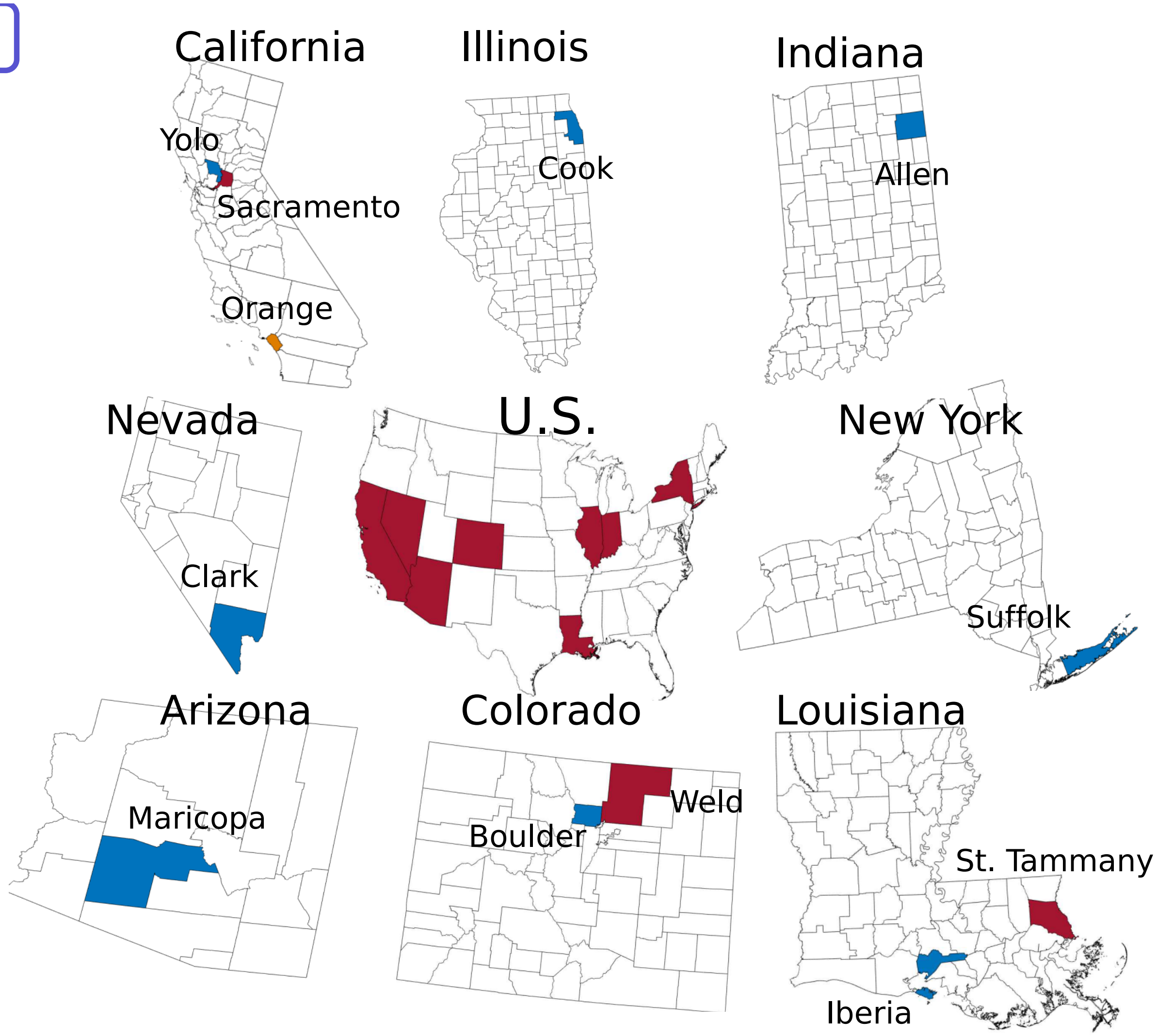
Background

Extrinsic Incubation Period



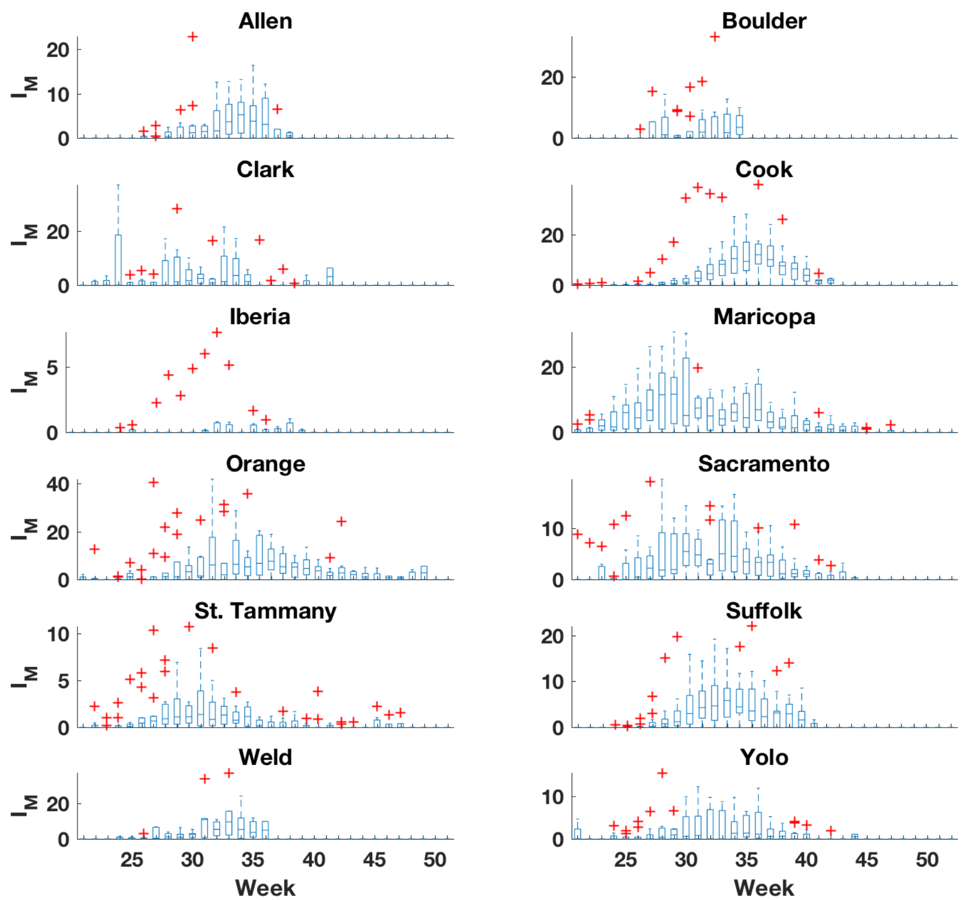
Vonnie D.C. Shields, 2017

Data


California
Yolo
Sacramento
Orange
Illinois
Cook
Indiana
Allen
Nevada
Clark
U.S.
New York
Suffolk
Arizona
Maricopa
Colorado
Weld
Boulder
Louisiana
St. Tammany
Iberia

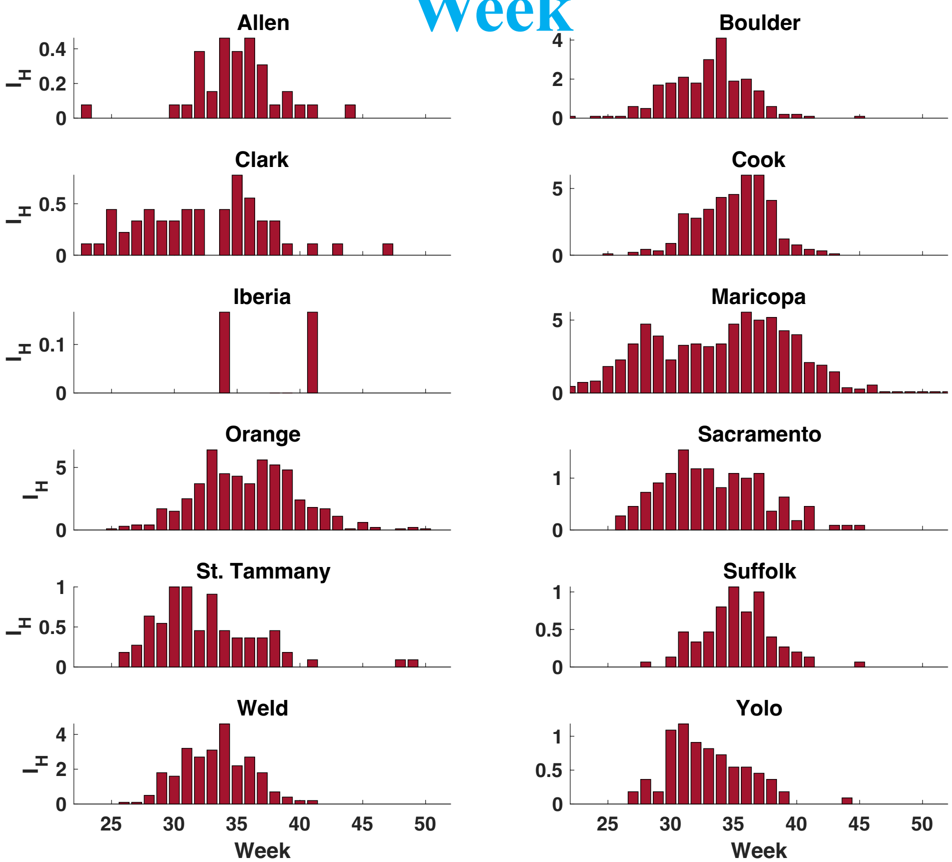
Surveillance Data

Weekly Infected Mosquitoes per 1,000 Tested



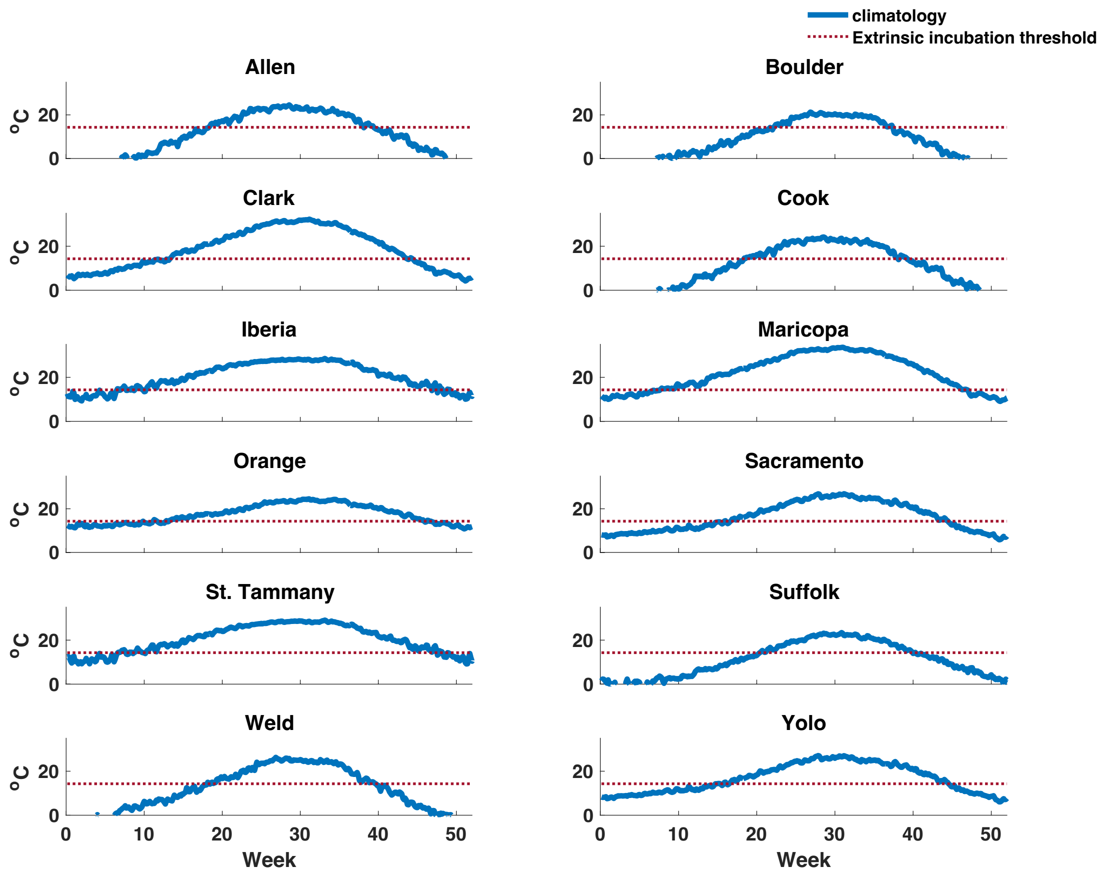
Surveillance Data

Average Observed Human WNV Cases by Week



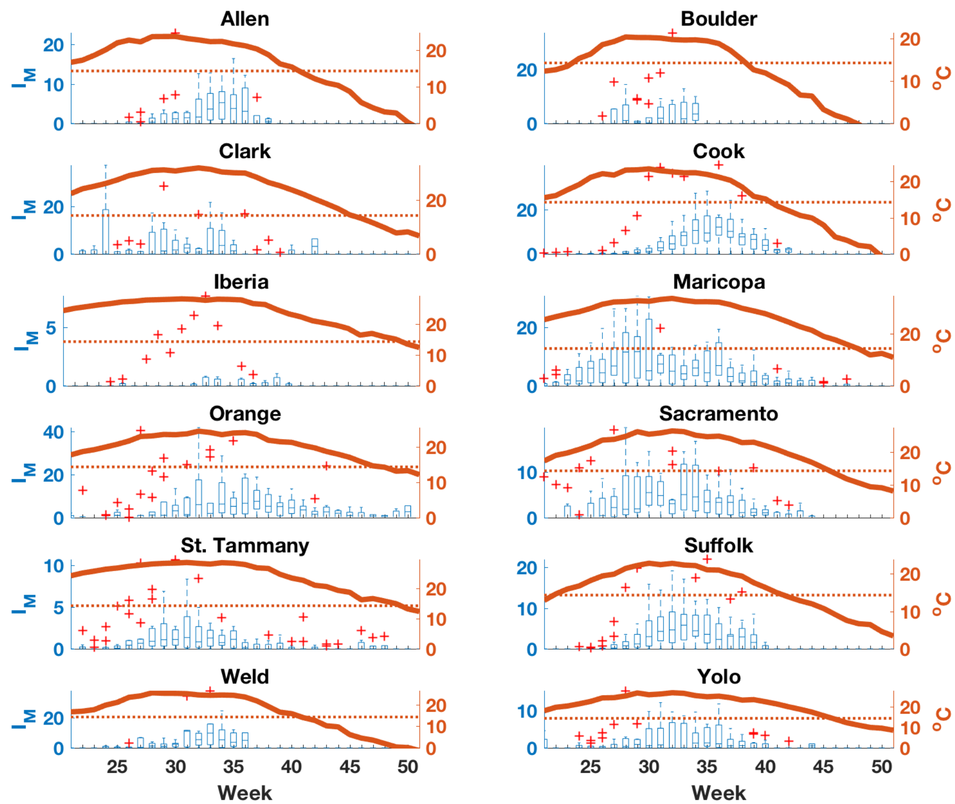
Data

Climatology



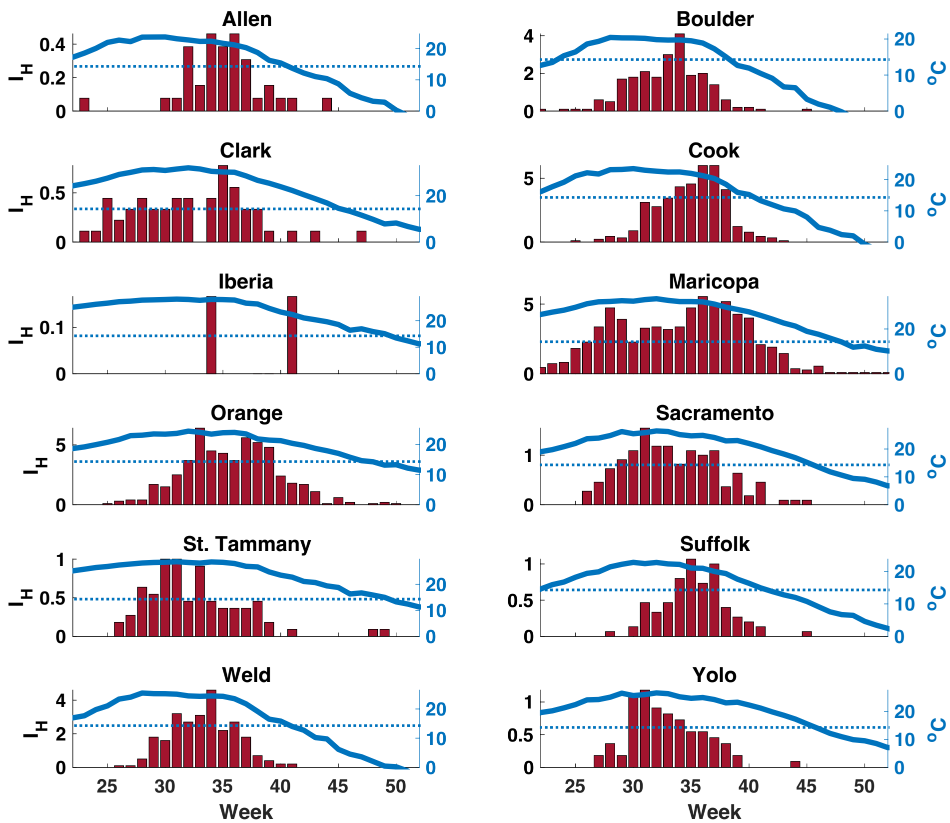
Data

atology and Infected Mosquitoes



Data

Climatology and Human Cases

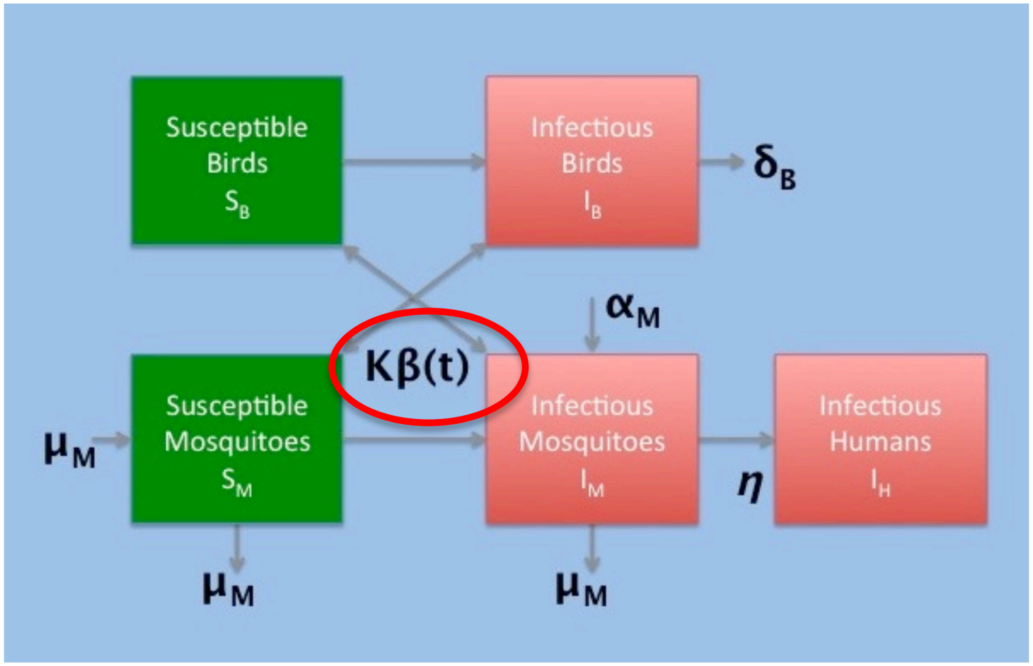


Model

Temperature Forced Compartmental Model

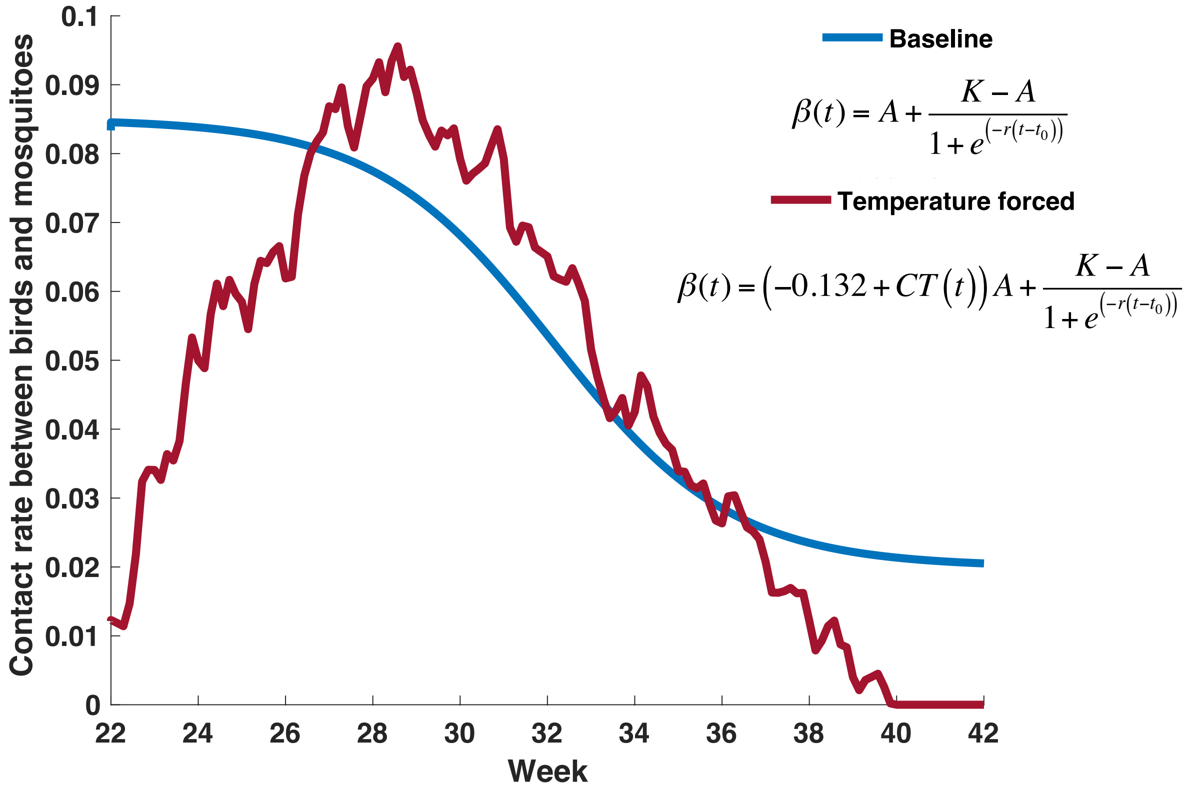
Parameters:

- μ_M – birth and death rate of mosquitoes
- δ_B – bird recovery rate
- $K\beta(t)$ – temperature forcing contact rate between birds and mosquitoes at time t
- η –risk of spill-over to humans
- α_M – rate of WNV seeding into the model domain



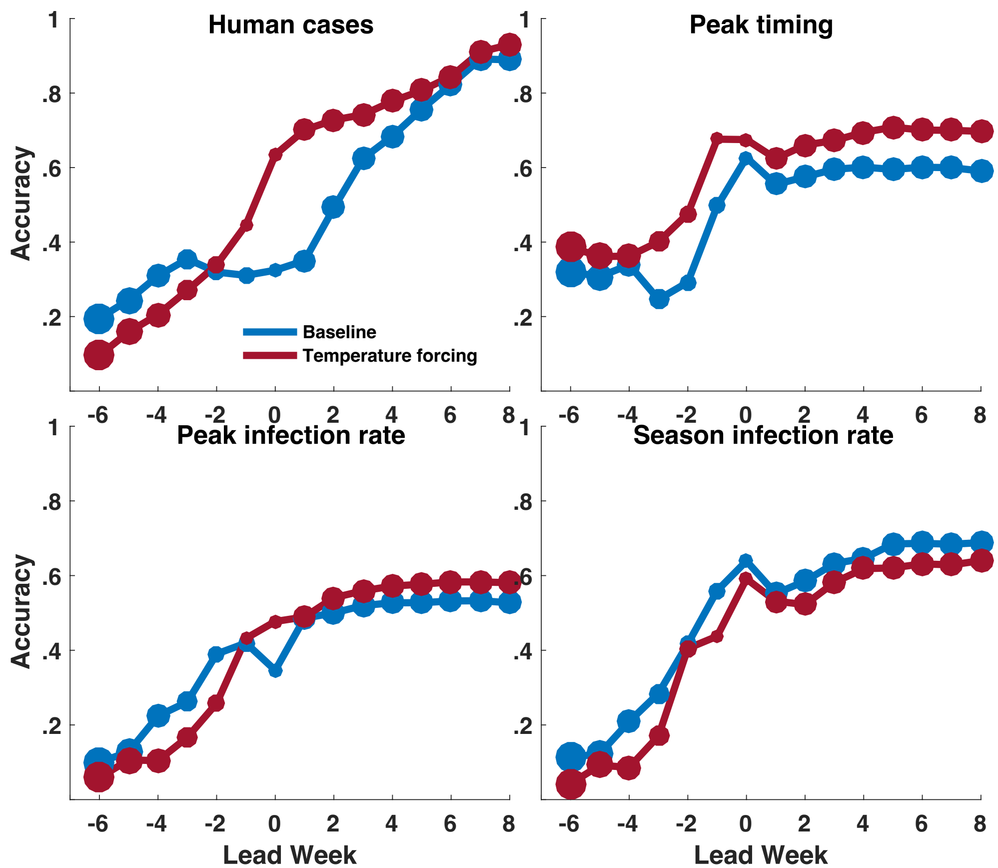
Model

Differences Between Baseline and Temperature Forcing



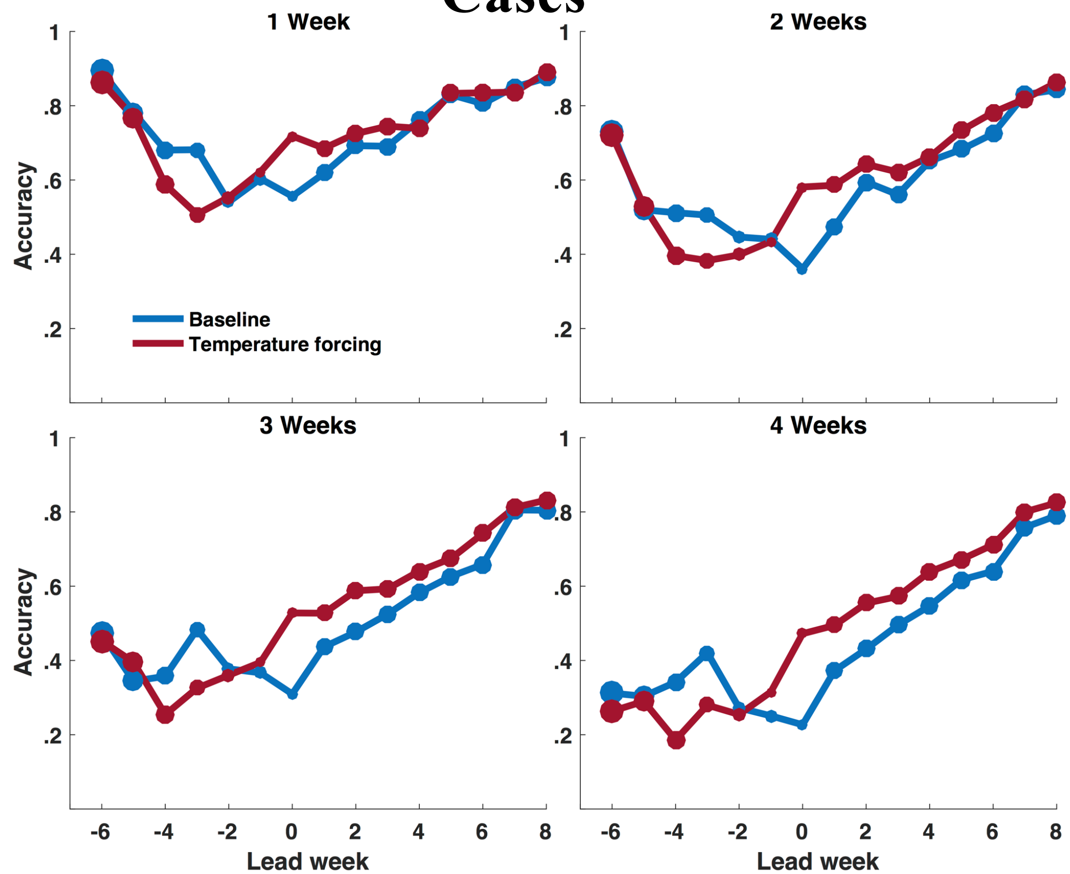
Results

Forecast Calibration Forecast Lead



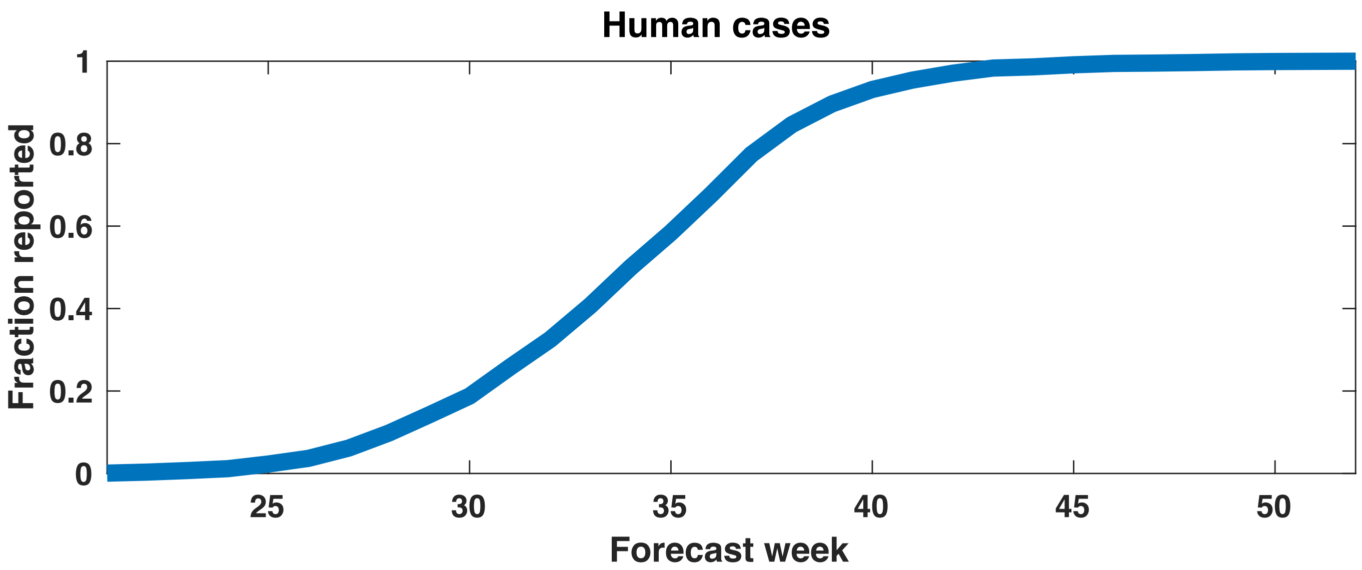
Results

Short-term Forecast Accuracy for Human Cases



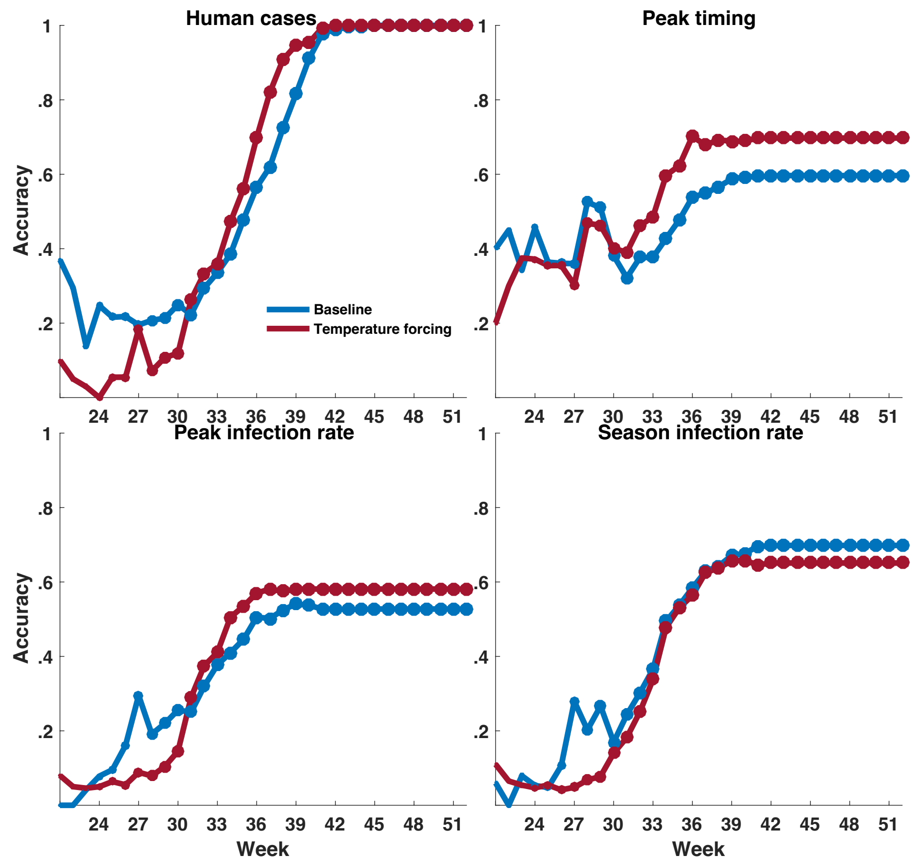
Data

Human Cases Forecast Week



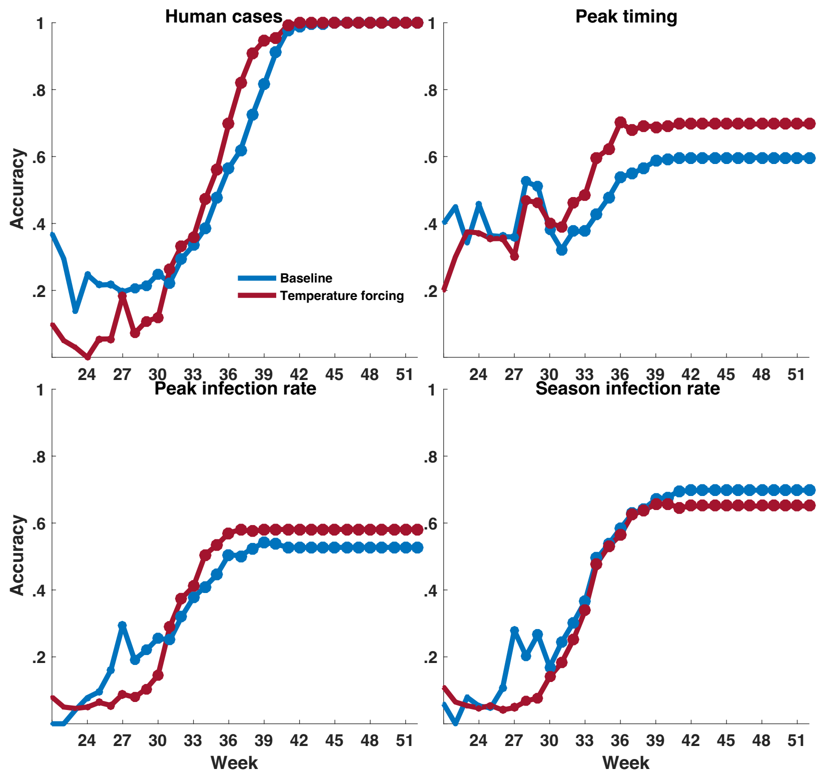
Results

Forecast Calibration Forecast Week



Results

Forecast Calibration Forecast Week



- Weeks 31 to 40:
  - Predicting human cases, 10%
  - Peak timing of infectious mosquitoes, 12%
  - Peak magnitude of infectious mosquitoes 6%

Results

- Up to a 9 week lead in predicting the last human case
- Accurately predict human cases prior to the majority of case being reported
  - 63% at peak of infectious
  - 70% 1 week past
  - 73% 2 weeks past
- Temperature-forcing model improves forecast accuracy in:
  - Predicating human cases, 10%
  - peak timing of infectious mosquitoes, 12%
  - peak magnitude of infectious mosquitoes 6%
    - Prior to the majority of the number of human cases reported
    - provide considerable advanced warning

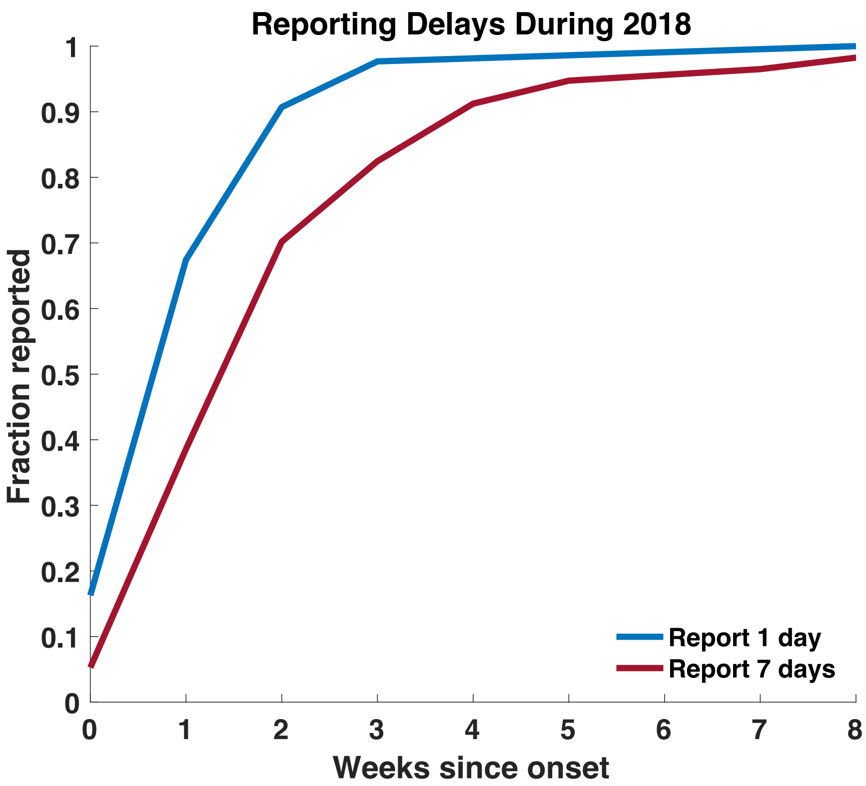
Implications

- Accurate retrospective forecasts of mosquito infection rates and human cases can be generated
- Foundation for a statistically rigorous system for real time forecasting
- Such a decision support tool would help public health officials and mosquito control programs:
  - Target control of infectious mosquito populations
  - Alert the public to future periods of elevated WNV spillover transmission risk
- This is the first step to a real-time forecast system of WNV

Data

What is Needed to Implement Real-time Forecasting?

Challenges related to real time forecasting:



Human WNV case reporting

- Human cases of WNV as a nationally notifiable disease
  - 7 days to report
  - only 51% were reported within 7 days[1]
  - California 1 day

[1]Boehmer *et al.* *2011*

Summary

- Meteorological conditions influence transmission
- Fluctuations in meteorological conditions can help identify risk areas
- Public health agencies and vector control use surveillance data and models to reduce outbreaks and hopefully reduce exposures
- Operational Real-time forecasting
  - **Key is reporting and confirming cases with limited delay**

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- Team:
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