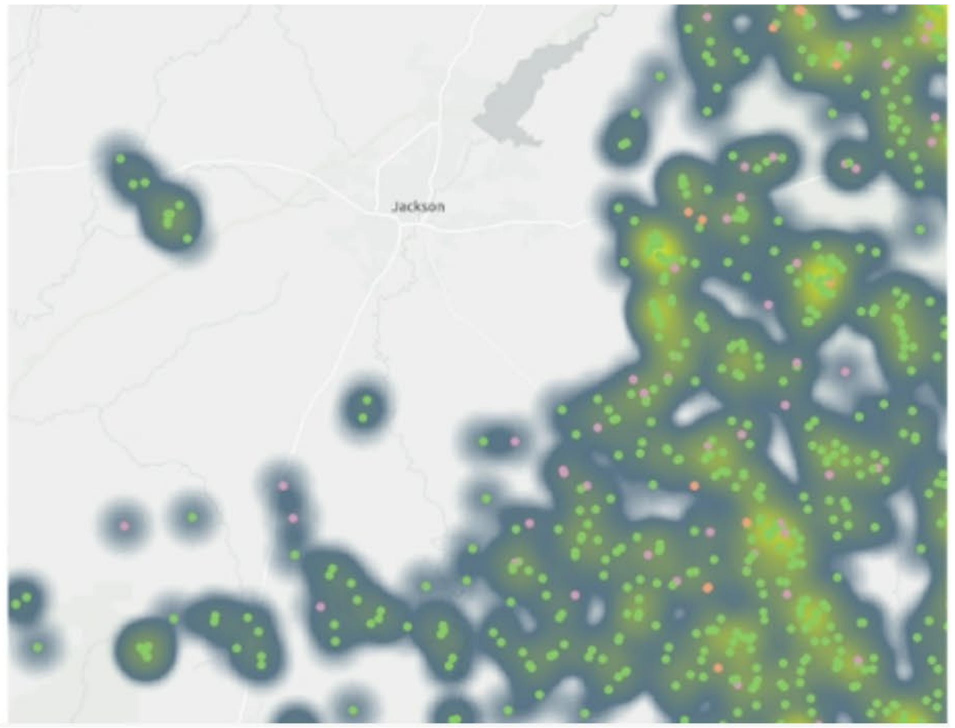
Developing Detection and Modeling Tools for the Geospatial and Environmental Epidemiology of Animal Disease



Mississippi State University
Cooperative Research Synthesis

USDA ARS Geospatial and Environmental Epidemiology Research Unit
May 2024 Scoping Workshop

MISSISSIPPI STATE UNIVERSITY

USDA Agricultural Research Service

Project PI’s

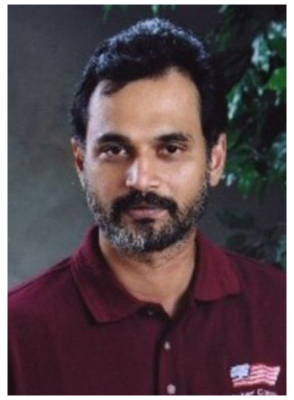
Kristine Evans, PhD
Associate Professor, Wildlife, Fisheries and Aquaculture
Associate Director, Geosystems Research Institute

Robert Moorhead, PhD
Professor, Electrical and Computer Engineering
Director, Geosystems Research Institute
Director, Northern Gulf Institute

Jamie Larson, PhD
Professor, Animal & Dairy Sciences
Associate Director, Mississippi Agricultural and Forestry Experiment Station

Bindu Nanduri, PhD
Professor, Comparative Biomedical Sciences, College of Veterinary Medicine

David Smith, DVM, PhD
Professor & Dean, Research and Graduate Studies, College of Veterinary Medicine



Mahalingam Ramkumar, PhD
Associate Professor, Computer Science and Engineering

Advancing Agricultural Research through High-Performance Computing

Developing Detection and Modeling Tools for the Geospatial and Environmental Epidemiology of Animal Disease

College of Veterinary Medicine:

Bindu Nanduri, PhD (Reducing Colonization of Salmonella In Poultry)

Isaac Jumper, DVM, PhD (Epidemiologic Approaches to Livestock Disease), (Cross Sectional Study to Determine Risk Factors for Anaplasmosis and Other Endemic Diseases of Cattle)

Kimberly Woodruff, DVM (Epidemiologic Approaches to Livestock Disease), (Rapid Testing for European Foul Brood in Honeybees)

David Smith, DVM, PhD (Use of Arthropods Vectors to Classify Cattle Herds by Anaplasmosis Infectious Status), (Test Performance of Normal Saline as a Transport Medium for Detection of *Tritrichomonas foetus* in Cattle Herds), (Diagnostic Approaches for Rapid Detection fo Herd-level Infections)

Department of Computer Science and Engineering

Mahalingam Ramkumar, PhD (Using Graph Neural Networks for Identifying Microbiome Signatures in Pastured Poultry)

Zhiquian Chen, PhD (Graph Neural Networks in Biology: A Case Study on MIC)

Nisha Pillal, PhD

Department of Poultry Sciences

Li Zhang, PhD (Minimizing Disease Transmission in Poultry through Rapid Detection and Predictive Models)

Department of Wildlife, Fisheries and Aquaculture

Melanie Boudreau, PhD (Optimizing Biologger Attachment and Retention in Channel Catfish (*Ictalurus punctatus*), (Using Biologging Technology to Understand Cattle) , (Seeing Through the Murky Waters: Understanding Catfish Disease Susceptibility as a Function of Behavior and Pond Environmental Conditions)

Dana Morin, PhD (Understanding the Role of Wildlife in the Spread of Antimicrobial Resistance)

Garrett Street, PhD (Impacts of Wild Animals on Agricultural Landscapes), (Monitoring Movement and Pollination Activities of Honeybees), (Using Computer Vision and Radar to Understand and Predict Parasite Spread)

Michael Sandel, PhD & Manuel Ruiz-Aravena, DVM, PhD (Optimizing One Health Surveillance Strategy for Zoonotic and Water-borne Bacterial Pathogens to Protect Animal and Human Health in Mississippi)

Department of Biochemistry, Molecular Biology, Entomology and Plant Pathology

Florencia Meyer, PhD (Recombination and Diversity in Bovine Coronavirus)

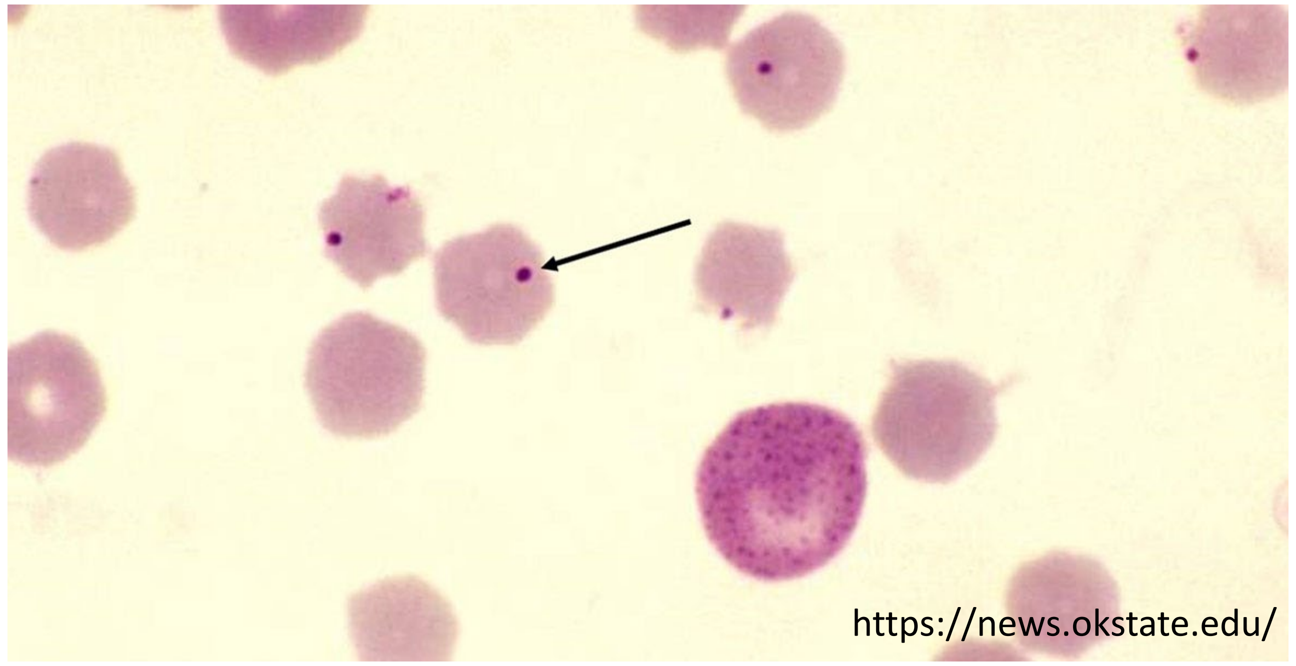
Department of Agricultural and Biological Engineering

Vitor Martins, PhD (Using Satellite Observations to Monitor Cropland and Water Resources), (Assessment of Landscape Disturbance and Climate Factors in Mapping Disease Transmission Risk near Open Cattle Feedlots)

Diagnostic approaches for rapid detection of herd-level infections

Bovine anaplasmosis (BA) caused by the obligate intraerythrocytic, rickettsial organism *Anaplasma marginale* is endemic in tropical and sub-tropical regions globally

- Estimated economic impact of $660 per clinically affected head in the United States
- BA induces production losses through several means. Infections of adult naïve cattle result in anemia, abortion, and acute death
- Infection of young calves establishes an inapparent carrier state where the animal may serve as a reservoir for infection



David R. Smith, DVM, PhD, Dipl. ACVPM, Dipl. Epidemiology

W. Isaac Jumper, DVM, PhD, Dipl. ACVPM

Kimberly A. Woodruff, DVM, MS, Dipl. ACVPM, Dipl. Epidemiology

Bindu Nanduri, PhD

Use of arthropod vectors to classify cattle herds by anaplasmosis infection status

Anaplasma marginale is endemic to the southeastern and northwestern United States

Tabanid flies as mechanical vectors

Dermacenter ticks as biological vectors

Anaplasma marginale organisms replicate in the tick.

https://bugguide.net/node/view/560099

Blood feeding transmits *Anaplasma marginale* directly from host to host

The goal is to determine whether a non-invasive method of sampling to detect *A. marginale* in free-living vector species, may be used to estimate the seroprevalence of anaplasmosis in cattle on the same pastures.

Objectives

- Determine the optimal sampling strategy for ***Dermacentor variabilis***
  - Estimate the proportion of *D. variabilis* among ticks captured by dragging
- Determine the optimal sampling strategy for **female tabanids**
  - Estimate the proportion of female tabanids among insects captured by H-trap
- Relate to seroprevalence of anaplasmosis in adjacent cattle herds

Cross-sectional study: estimate prevalence and identify risk factors associated with diseases of beef cattle in Mississippi

- W. Isaac Jumper, DVM, PhD, Dipl. ACVPM
- Carla L. Huston, DVM, PhD, Dipl. ACVPM, Dipl. Epidemiology
- Brandi B. Karisch, PhD, Animal and Dairy Sciences
- David R. Smith, DVM, PhD, Dipl. ACVPM, Dipl. Epidemiology

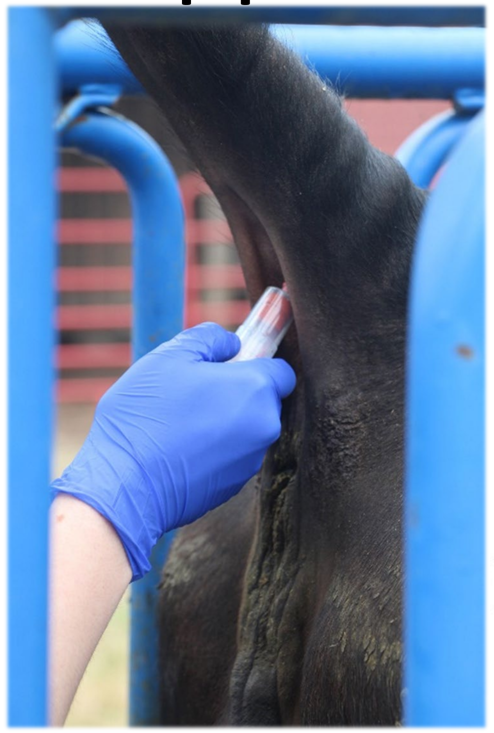
- In 2023, 860,000 beef cattle on 15,980 farms in Mississippi. 5th largest agriculture commodity in MS
- Prevalence and risk factors for some production-limiting diseases are not well known
  - Bovine anaplasmosis
  - Bluetongue virus
  - Bovine leukemia virus
  - *Neospora caninum*
  - Leptospirosis
  - Bovine Viral Diarrhea Virus

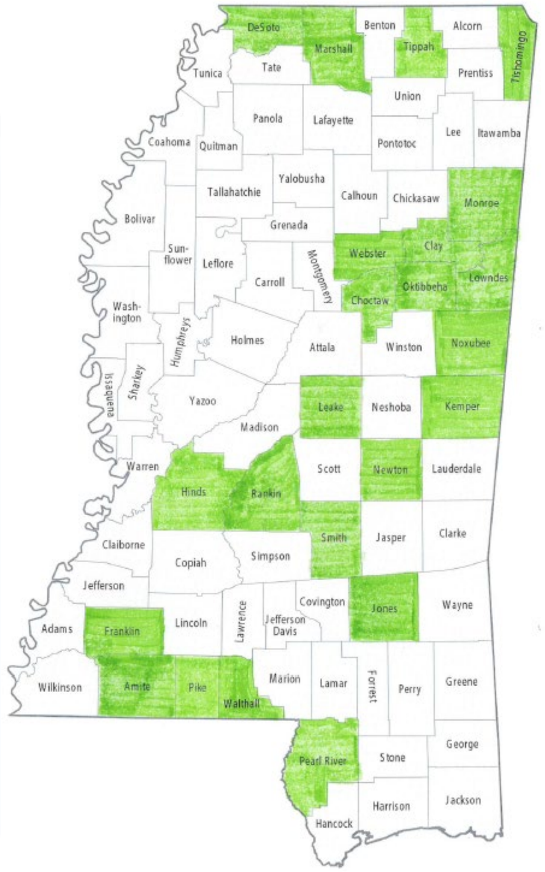
Objective

- Describe within and between herd prevalence, geographical distribution, as well as management and biosecurity risk factors for various production-limiting diseases of beef cattle in Mississippi

Status of sample collection

- Blood samples collected from cattle in 40 herds in 23 counties across the state
  - 2,112 total serum samples collected
- Initial sample size calculations have been met (n=40)
  - Sample collection will continue as herds are available
- Serum testing currently underway





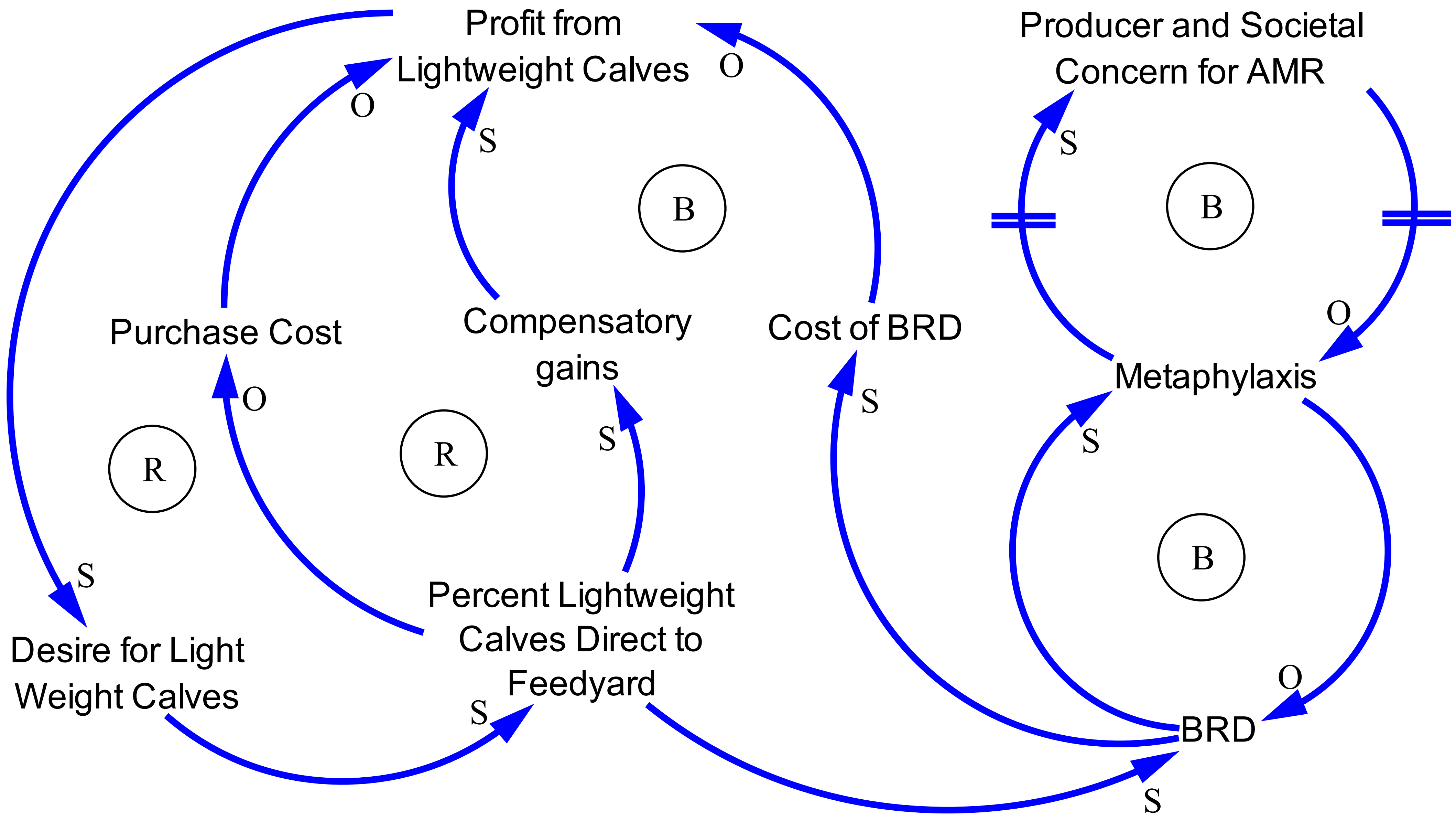
Preliminary results

- 17/20 herds had at least 1 animal test positive
  - 3 herds had 0 animals test positive
- Antimicrobials may be used to treat disease or mitigate risk
  - In-feed antimicrobial use raises stewardship concerns

Impact of feeding chlortetracycline (CTC) on BA seroprevalence

Univariable Model	Variable Level	Responses	Estimate Value	Standard Error	Odds Ratio	95% CI		P-Value
Intercept			-1.0296	0.4505				
CTC Free-Choice Mineral Usage								
	Yes	9	1.2088	0.5114	**3.349**	1.229	9.126	**0.0221**
	No	11	Ref.	Ref.				

What is the effect of policies against the use of antimicrobials in beef production on profit and animal well-being?



System dynamics model of beef production antimicrobial stewardship

Some cattle feeders desire lightweight calves despite increased risk for pneumonia. The problem is currently mitigated with mass antimicrobial therapy

Test performance of normal saline as a transport medium for detection of *Tritrichomonas foetus* in cattle herds by qRT-PCR

David R. Smith, DVM, PhD, Dipl. ACVPM, Dipl. Epidemiology

Obligate extracellular protozoan

Venereal transmission

Clinical signs → reproductive losses

Bull = asymptomatic carrier

Economic impact

$650 million annually (Speer CA, 1991)

$44,000/ year for cow-calf producer (Anderson, 2014)

No FDA approved treatment

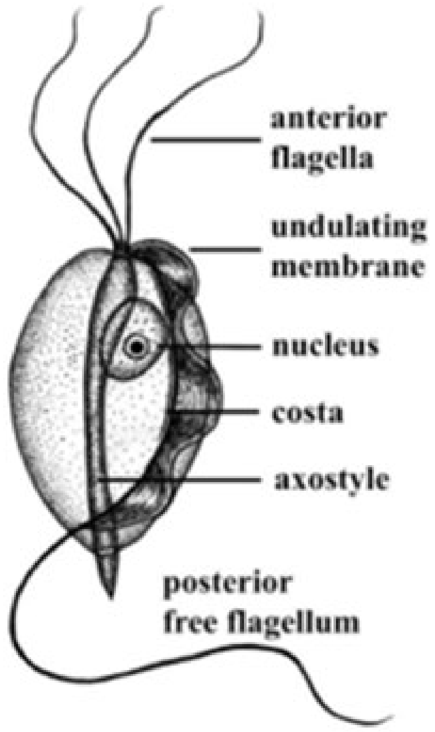


Image courtesy of Google Images

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COLLEGE OF ENGINEERING

Machine Learning/Deep Learning/Graph Neural Networks

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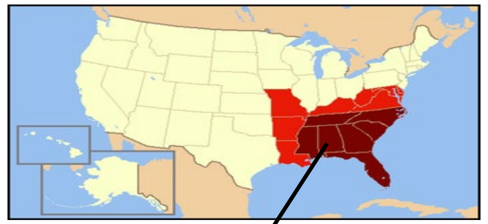
Zhiqian Chen, PhD
Nisha Pillai, PhD
Dept. Of Computer Science and Engineering

Bindu Nanduri, PhD
College of Veterinary Medicine

Moses B Ayoola PhD, Santhanakrishnan Boopalan PhD, Athish R Das MS, Ganga Gireesan MS

Preharvest Environmental and Management Drivers of Multi-Drug Resistance in Major Bacterial Zoonotic Pathogens in Pastured Poultry Flocks

Dataset



11 Southeastern Poultry Farms

Feces

Soil

31 Farm Practices + 24 Physiochemical Properties Collected for Each Sample

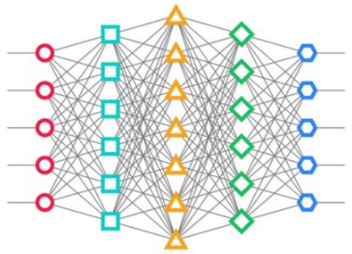
Approach

Influential Variables

SHAP Predicts direction

Bagging (≥3 Algorithms Agree)

1. RandomForest
2. XGBoost
3. MLP
4. Autoencoder
5. GAN



Machine/Deep Learning

Influential Elements

Salmonella

- Phosphorus
- Low pH
- Low EC
- High Manganese
- Low Sodium

Listeria

- Magnesium
- Phosphorus
- Flock Size
- Potassium
- Copper
- YearsFarming

Michael J. Rothrock, PhD
USDA-ARS
Athens, GA

Microorganisms 2022, 10(9), 1703

Dataset

- Pastured Poultry
  - Management Practices, Soil physicochemical properties
  - Food safety: zoonotic bacterial pathogens
  - Antibiotic Resistance, MDR
  - Microbiome

Models

- Models for pathogens (*Campylobacter, Listeria, Salmonella*), MDR
  - Ensemble approach
  - Pair-Difference model
    - ($N \times M$ to $N^2 \times 2M$)
- Explainable AI
  - Order of importance
  - Combinatorial optimization
    - Important feature pairs
    - Important triplets
    - …

- Deep sensitivity analysis for objective-oriented *combinatorial optimization*. International Conference on Computational Science & Computational Intelligence (CSCI'23)
- Towards *Interpreting Multi-Objective Feature* Associations, International Systems Conference (IEEE SysCon 2024)

- Predicting foodborne pathogens and probiotics taxa within poultry-related *microbiomes* using a machine learning approach. Anim Microbiome. 2023
- Towards optimal *microbiome* to inhibit multidrug resistance. IEEE Conference on Computational Intelligence in Bioinformatics and Computational Biology (CIBCB) 2023.
- Bayesian-Guided Generation of Synthetic *Microbiomes* with Minimized Pathogenicity. International Conference of the IEEE Engineering in Medicine and Biology Society (IEEE EMBCm 2024)

- EndToEndML: An Open-Source End-to-End *Pipeline* for Machine Learning Applications. International Conference on Information and Computer Technologies (ICICT 2024, March 15-17).

- **NARMS**
    - Antibiotic Resistance (250000 samples)
    - 4500 nontyphoidal *Salmonella* whole genome sequences
    - MIC for 15 antibiotics

Antibiotic	Target	Resistance Genes Group
Ampicillin	Cell Wall	β-lactam
Amoxicillin-clavulanic acid	Cell Wall	β-lactam
Ceftriaxone	Cell Wall	β-lactam
Azithromycin	Protein	Macrolide
Chloramphenicol	Protein	Phenicol
Ciprofloxacin	DNA	Quinolone
Trimethoprim-Sulfamethoxazole	DNA	Sulfonamide
Sulfisoxazole	DNA	Sulfonamide
Cefoxitin	Cell Wall	β-lactam
Gentamicin	Protein	Aminoglycoside
Kanamycin	Protein	Aminoglycoside
Nalixidic acid	DNA	Quinolone
Streptomycin	Protein	Aminoglycoside
Tetracycline	Protein	Tetracycline
Ceftiofur	Cell Wall	β-lactam

NARMS
National Antimicrobial Resistance Monitoring System

The National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS) was established in 1996. NARMS is a collaboration among state and local public health departments, CDC, the U.S. Food and Drug Administration (FDA), and the U.S. Department of Agriculture (USDA).

This national public health surveillance system tracks changes in the antimicrobial susceptibility of certain enteric (intestinal) bacteria found in ill people (CDC), retail meats (FDA), and food animals (USDA) in the United States. The NARMS program at CDC helps protect public health by providing information about emerging bacterial resistance, the ways in which resistance is spread, and how resistant infections differ from susceptible infections.

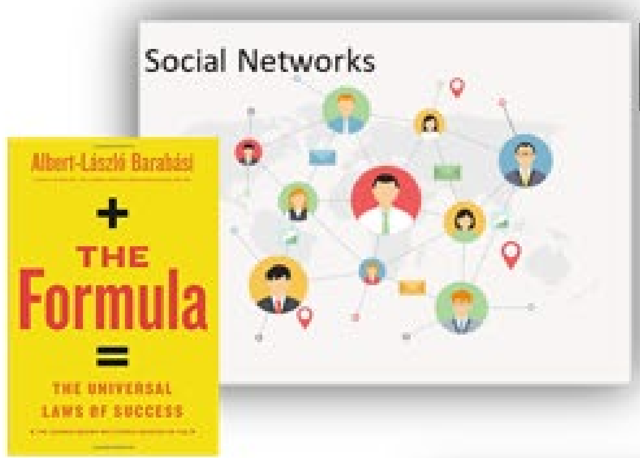
Traditional machine learning (random forest) with deep learning models (multilayer perceptron and DeepLift) for WGS-based MIC prediction using K-mers.

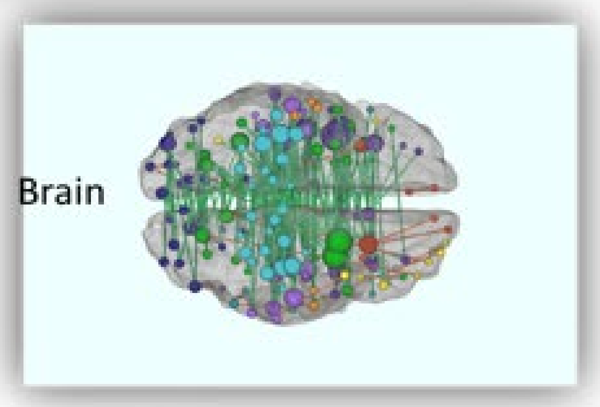
- Predicting *Salmonella* MIC and deciphering genomic determinants of antibiotic resistance and susceptibility. Microorganisms. 2024; Jan 10; 12(1): 134

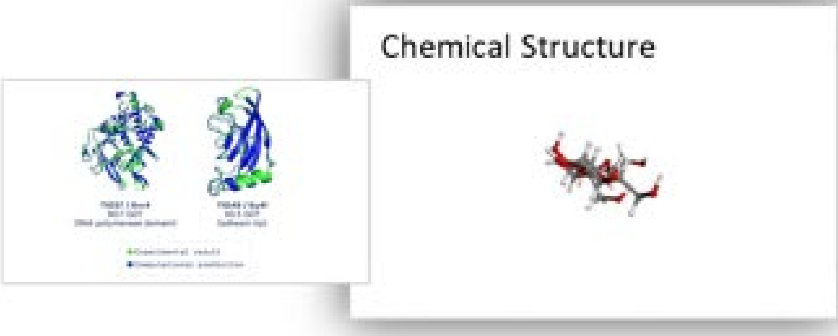
Graph is Everywhere

Graph dynamics
Disease spread

Epidemic



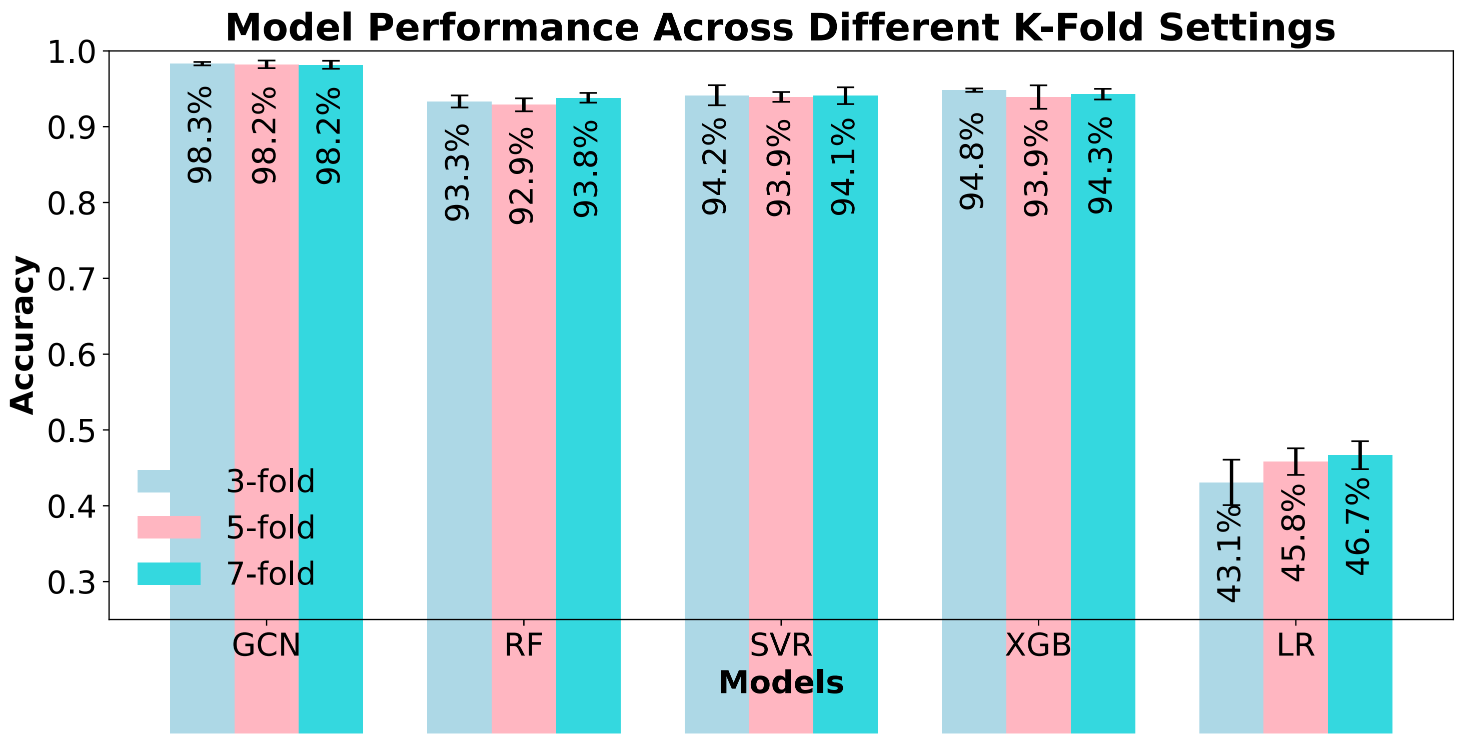




Graph Neural Networks (GNN) for MIC Prediction

- GNNs offer advantages over conventional ML methods by incorporating connectivity, topology, and non-Euclidean data into the learning process.

- K-mer GNN model
  - Nodes are k-mers, edges show sequence similarity
  - Encodes k-mer presence/absence as features
- Integrates graph structure and sequence data
  - Allows predicting MICs and understanding resistance
- Evaluated *Salmonella* MIC prediction model by conducting comparative analyses with including Linear Regression, Random Forest Regressor (RF), Support Vector Regressor(SVR), and XGBoost (XGB).

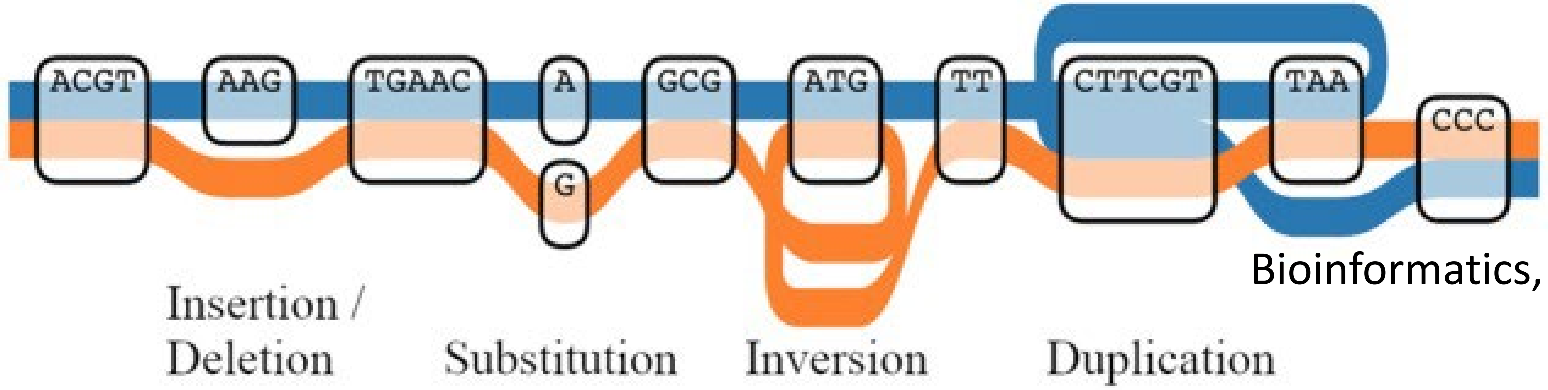


- Leveraging Graph Neural Networks for MIC Prediction in Antimicrobial Resistance Studies. International Conference of the IEEE Engineering in Medicine & Biology Society, 2024

Ongoing / Planned Work

Fda.gov/food/foodborne-pathogens/salmonella

- *Salmonella* genomes (over 550,000)
    - Pan Genome Graph



Bioinformatics, 2019

    - 80,000 with labelled MIC
        - 6000 in NARMS

LLM for *Salmonella*

- Purpose: a core model to allow fine tuning of smaller models
- Not trained to just predict next / missing token
    - Predict all available labels
    - API for going from genome subsequence (in a sample window) to trainable labels
- Pros and Cons of generative (GPT like) or predictive (Bert-like)

- GNN for serotype prediction

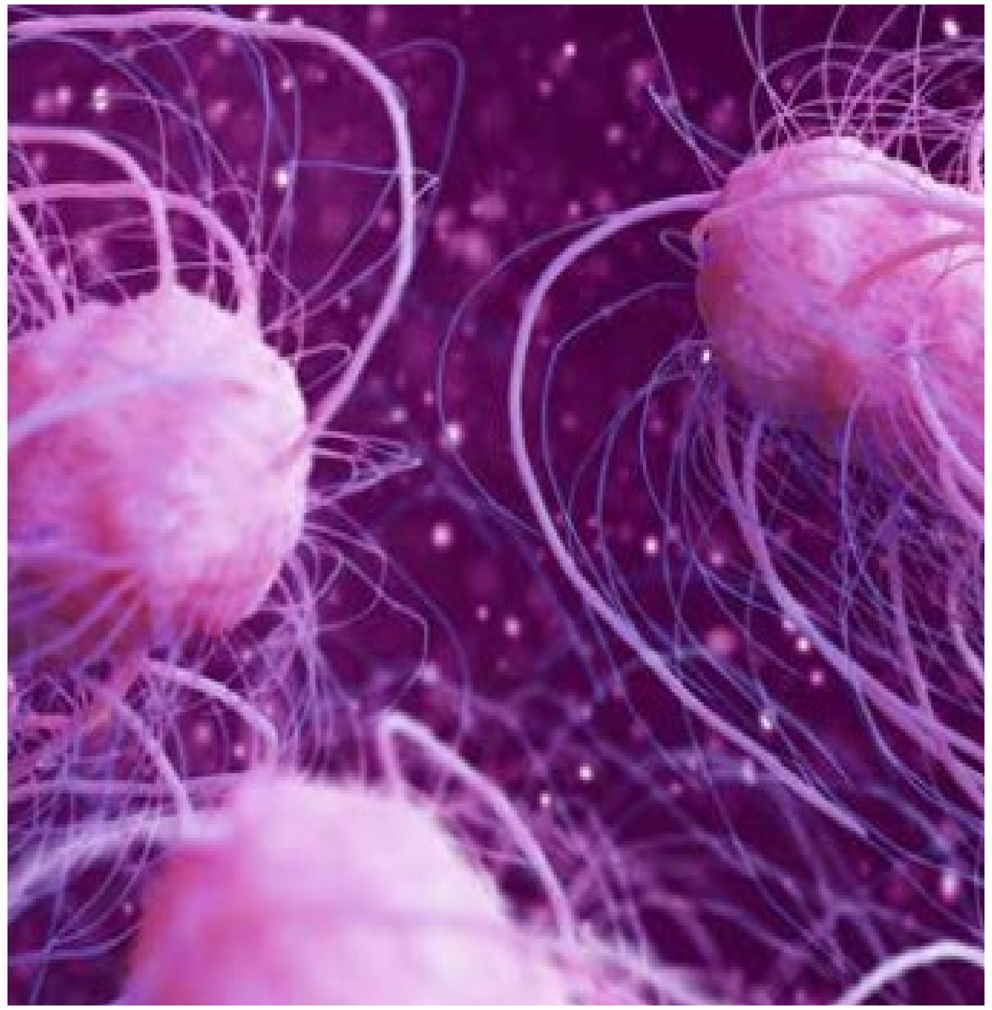
USDA-ARS : Adam Rivers, GBRU, GEERU, Gainesville, FL Jonathan Frye, Athens, GA.

LLM for Microbiomes

Science of the Microbiome

The collective genomes of all the microbes (bacteria, fungi, viruses, et al.) in a human, plant, animal, or environmental community have tremendous potential. The microbiome for plants affects productivity as well as stress and disease resistance. A cow's microbiome can influence the amount of methane produced by the animal. A soil's microbiome can be enhanced for more nutritious crops, to sequester more carbon, to capture more water, or to prevent erosion. Microbiomes maintain the healthy function of these diverse ecosystems and influence human health, climate resiliency, food security, and other important and critical phenomena.

USDA Science Blueprint 2020-2025



- Variety of small microbiome abundance data available
  - From a wide range of unrelated experiments
  - Different types of samples
  - Different species, soil, feces

USDA-ARS: Michael J. Rothrock & Adelumola Oladeinde , Athens, GA, Laxmi Yeruva, Little Rock, AR

Transformers for Tabular Data

- ML models ignore the deeper meaning of “features”
  - Input variables like temperature, salinity, *E. coli* CFUs, etc., are just x_1, x_2,.. x_n for the model
  - Are reasonably good *embeddings* possible for various features?
  - Using data created for possibly unrelated and even unknown purposes…
- Better explainability
  - Attention matrix can be interpreted as an edge graph showing transition probabilities
  - A model for feature importance (calculable for every sample) using PageRank

- Exploring Pathogen Presence Prediction in Pastured Poultry Farms through Transformer-Based Models and Attention Mechanism Explainability. (Ready for submission)

Michael J. Rothrock, USDA-ARS, Athens, GA.

Realtime Animal Health Monitoring

Current Research: Real-time pasture surveillance tool using drones and remotely sensed data

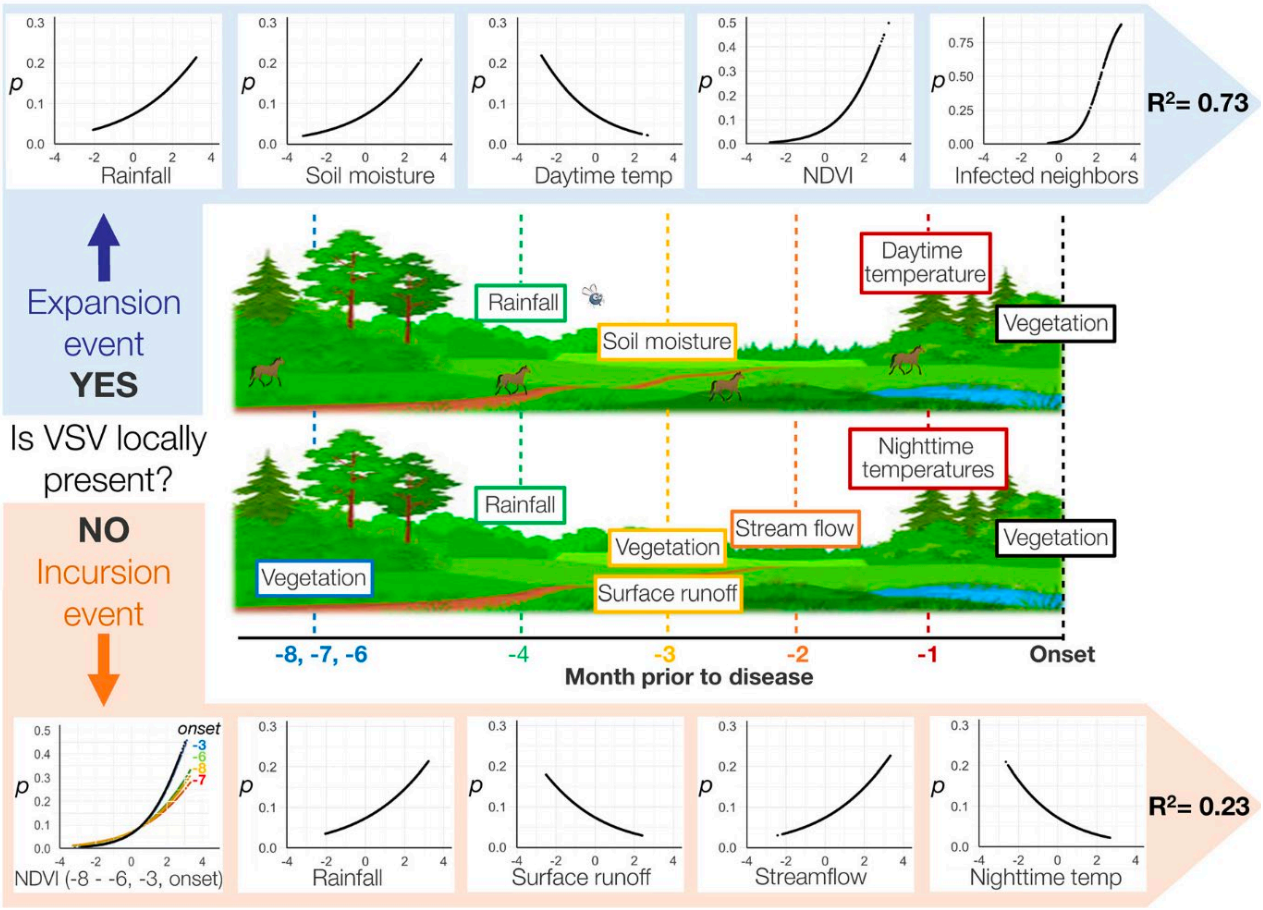
- Animal counts, weight, and body temperature
- Mass and nutritional value
- Thermal, hyper, 3-D, and multispectral data
- Convolutional Neural Networks, Vision Transformers

Objective: Develop Artificial Intelligence based Smart Tools for Farmers for detecting animal disease and responding to animal welfare challenges

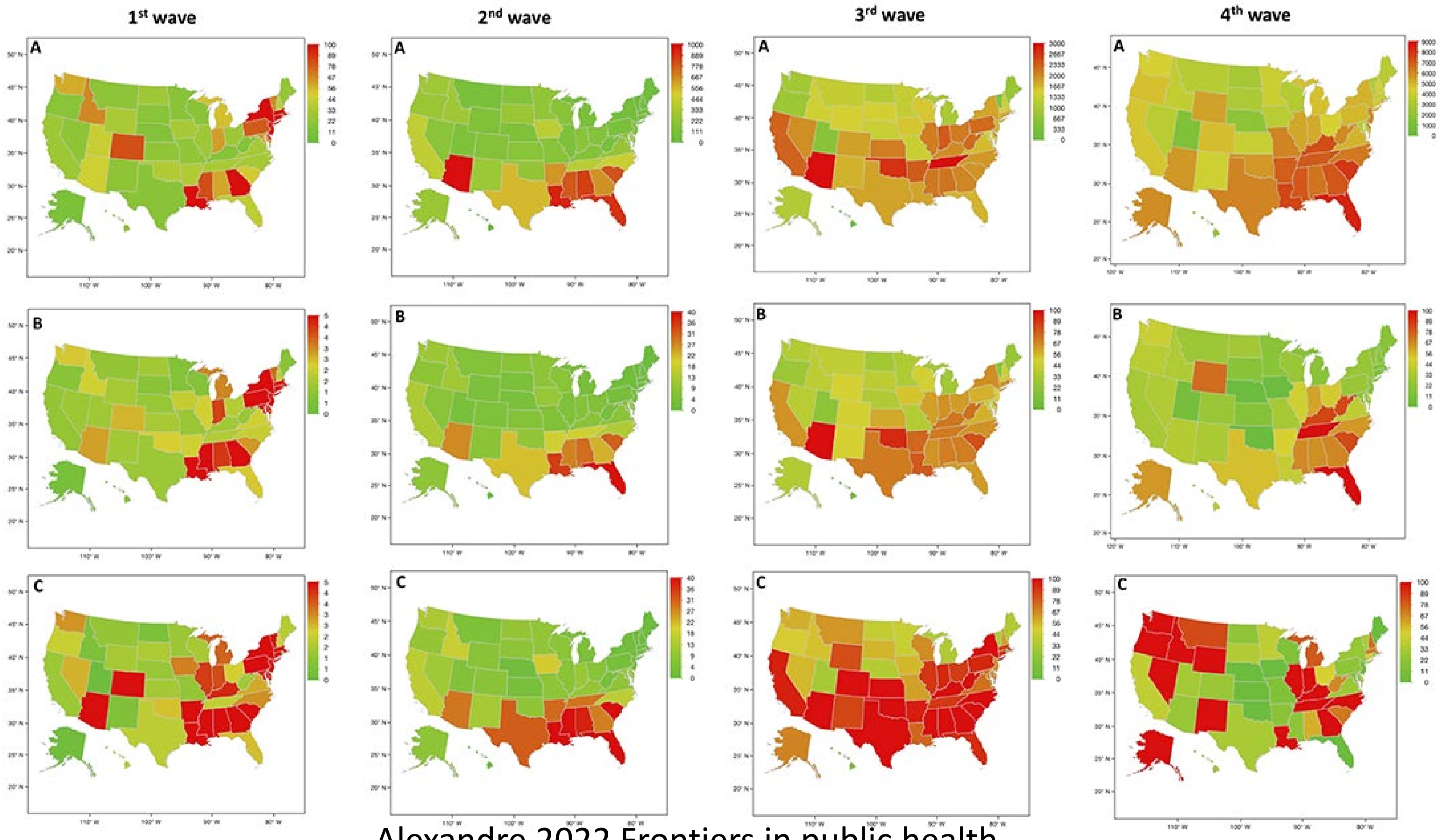
Amanda Ashworth, USDA-ARS, Fayetteville, AR.

Spatial Modeling the Spread of Vesicular Stomatitis (VS)

- **Research**: When will VS enter the US? Once VS does spread into the US, where will it go next?
  - Microcosmic: temperature, soil moisture, vegetation, etc
  - Macroscopic: geospatial propagation patterns



Peters et al. 2020 Ecosphere



Alexandre 2022 Frontiers in public health

Microcosmic: ecological factor **+** **Macroscopic: Geospatial patterns**

Amy R Hudson, USDA-ARS, Manhattan, KS.

Research Plan

- **To integrate Macroscopic and Microcosmic factors**
  - **Epidemic Modeling with Spatial Constraints**: Integrate traditional epidemiological models, such as the SIR with spatial graph structures.
- **To reduce the data demand**
  - **Bayesian Inference for spatial graph**: Employ Bayesian inference techniques to quantify the uncertainty in disease spreading predictions and model parameters. This could involve developing hierarchical Bayesian models or using Markov Chain Monte Carlo (MCMC) methods to estimate posterior distributions over the model parameters, accounting for spatial and temporal uncertainties.
- **To unify and utilize different data granularities**
  - **Multi-Scale Modeling**: Develop multi-scale models that capture disease spreading at different spatial resolutions, from individual-level interactions to regional or global-scale dynamics. This could maximize the utilization of data collected from every level.
- **To provide scientific conclusion**
  - **Causal Inference and Intervention Modeling**: Explore causal inference techniques to identify the causal factors and interventions that can effectively mitigate disease spreading in spatial networks. This could involve methods like causal graphical models, counterfactual reasoning, or structural equation modeling, enabling the development of targeted interventions and policy recommendations.

- Mississippi #1 in catfish production in U.S. (39,000 acres).
- >$200 million annually contributed to Mississippi agriculture by honeybees.
- ~910,000 head of cattle on 15,980 farms in Mississippi.
- Mississippi #10 in US broiler production, >715 million broilers

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DEPARTMENT OF WILDLIFE, FISHERIES AND AQUACULTURE

Investigators: Melanie Boudreau, Garrett Street, Mike Sandel, Peter Allen (MSU-WFA)
Brian Ott (USDA-ARS)
Matthew Griffin (MSU-CVM)

Project: *Seeing Through the Murky Waters: Understanding Catfish Disease Susceptibility as a Function of Behavior and Pond Environmental Conditions*

Objectives:

#1: Calibrate and translate accelerometer signals and acoustic recorders to identify behaviors and track catfish movement throughout ponds

#2: Quantify catfish behavior, physiology, and movement in relation to environmental conditions (e.g. low oxygen) in pond environments

#3: Quantify disease community composition in ponds over time (in water and on fish)

#4: Quantify the role of the environment and catfish responses in disease susceptibility

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DEPARTMENT OF BIOCHEMISTRY, MOLECULAR BIOLOGY, ENTOMOLOGY & PLANT PATHOLOGY

Investigators: Florencia Meyer, Federico Hoffman (MSU-BCH)
Roberto Palomares (UGA)
Aspen Workman (USDA-ARS)

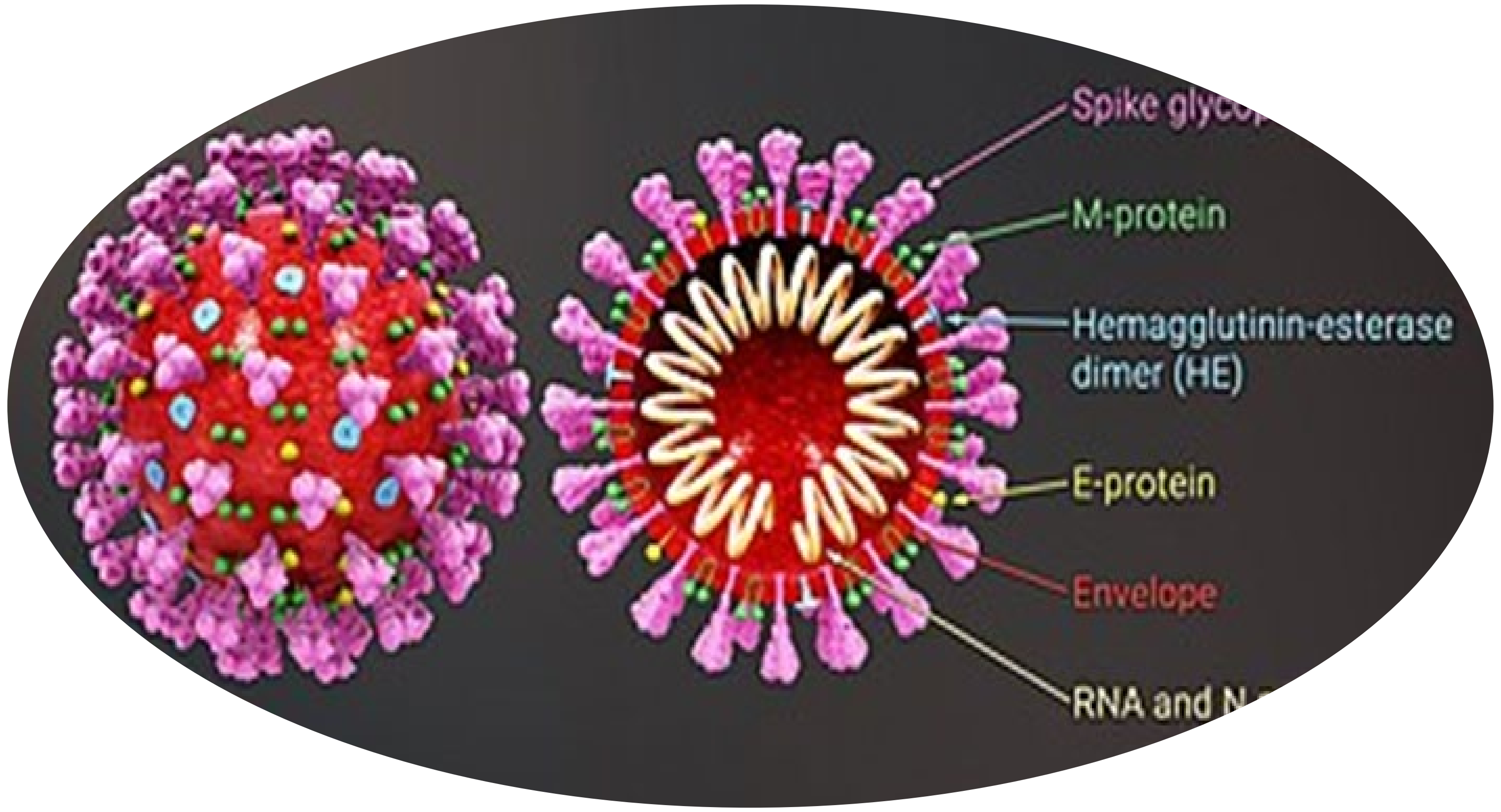
Project: *Recombination and diversity in Bovine Coronavirus*

Objectives:

#1: Longitudinal sampling to track molecular changes over time (Mississippi & Georgia dairy herds; Nebraska beef herds)

#2: Evaluate role of recombination in generation of novel viral genotypes

#3: Evaluate the role of management practices in differences in viral diversity



MISSISSIPPI STATE UNIVERSITY™
DEPARTMENT OF AGRICULTURAL AND BIOLOGICAL ENGINEERING

Investigators: Vitor Martins (MSU-ABE)

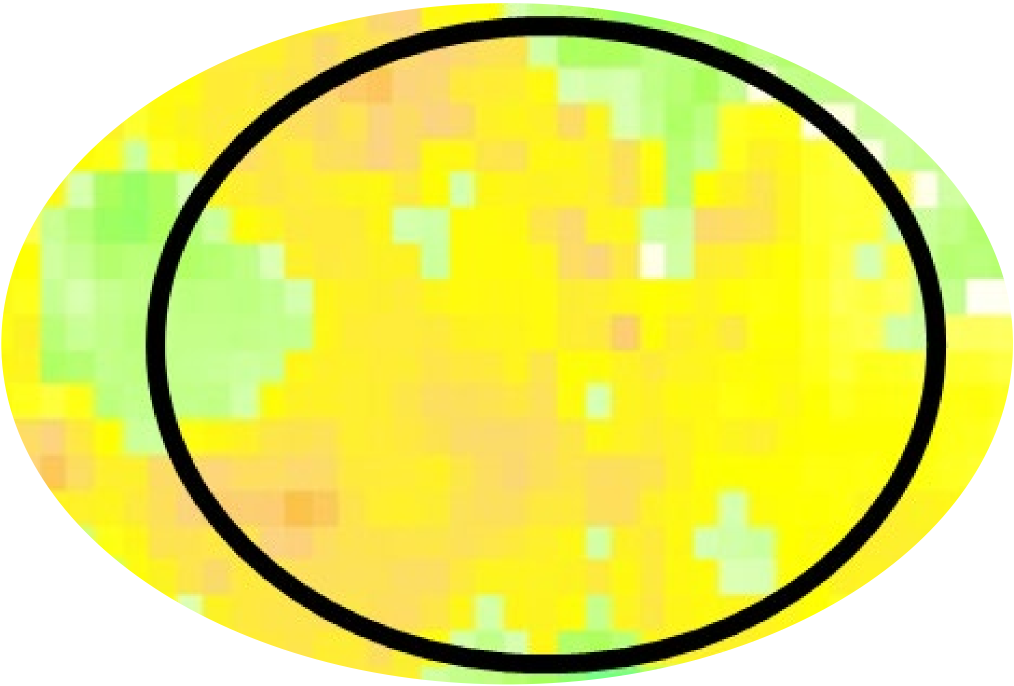
Project: *Assessment of landscape disturbance and climate factors in mapping disease transmission risk near open cattle feedlots*

Objectives:

#1: Build baseline information with geographic locations of open feedlots in North Carolina and Texas with visual interpretation and object detection in NAIP images

#2: Integrate a set of landscape and climate variables derived from satellite and ground observations for spatial modeling

#3: Develop geospatial modeling for hotspot mapping of disease transmission risk in the open cattle feedlots



MISSISSIPPI STATE UNIVERSITY™
DEPARTMENT OF POULTRY SCIENCE

Investigators: **Li Zhang, Ken Macklin (MSU-PS)**
Chuan-Yu Hsu, Mark Arick (MSU-IGBB)

Project: *Minimizing disease transmission in poultry through rapid detection and predictive models*

Objectives:

#1: Develop dataset through genomic analysis of avian pathogens

#2: Establish analysis pipeline via detection tools development

#3: Predictive modeling for poultry disease forecasting

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JAMES WORTH BAGLEY COLLEGE OF ENGINEERING

Investigators: Garrett Street, Melanie Boudreau (MSU-WFA)
Elizabeth Walsh (USDA-ARS)
John Ball, Ryan Green, Ali Gurbuz, Junming Diao (MSU-ECE)

Project: *Using computer vision and radar to understand and predict parasite spread*

Objectives:

#1: Identify critical mechanisms contributing to robbing events and directional movements of *Varroa* between robbing and robbed colonies

#2: Quantify colony health with respect to *Varroa* infestation, robbing events, bee movements, colony proximities, and habitat conditions

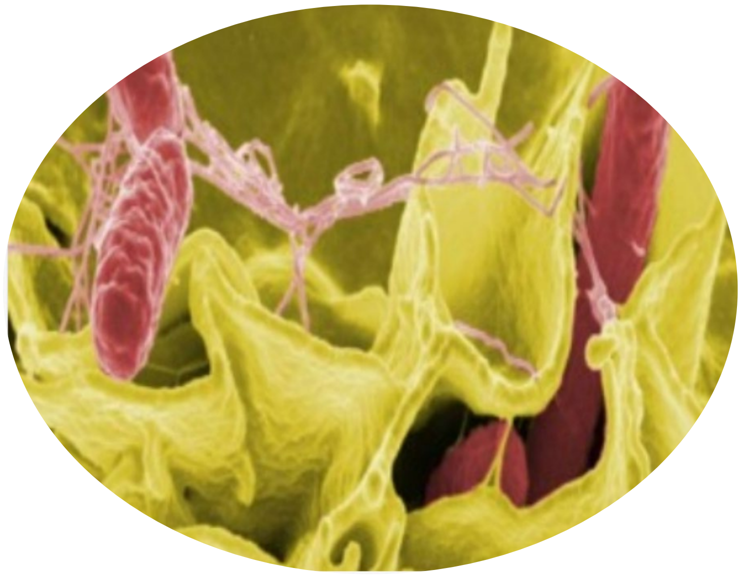
#3: Deployment a passive harmonic radar to monitor movements tagged honeybees

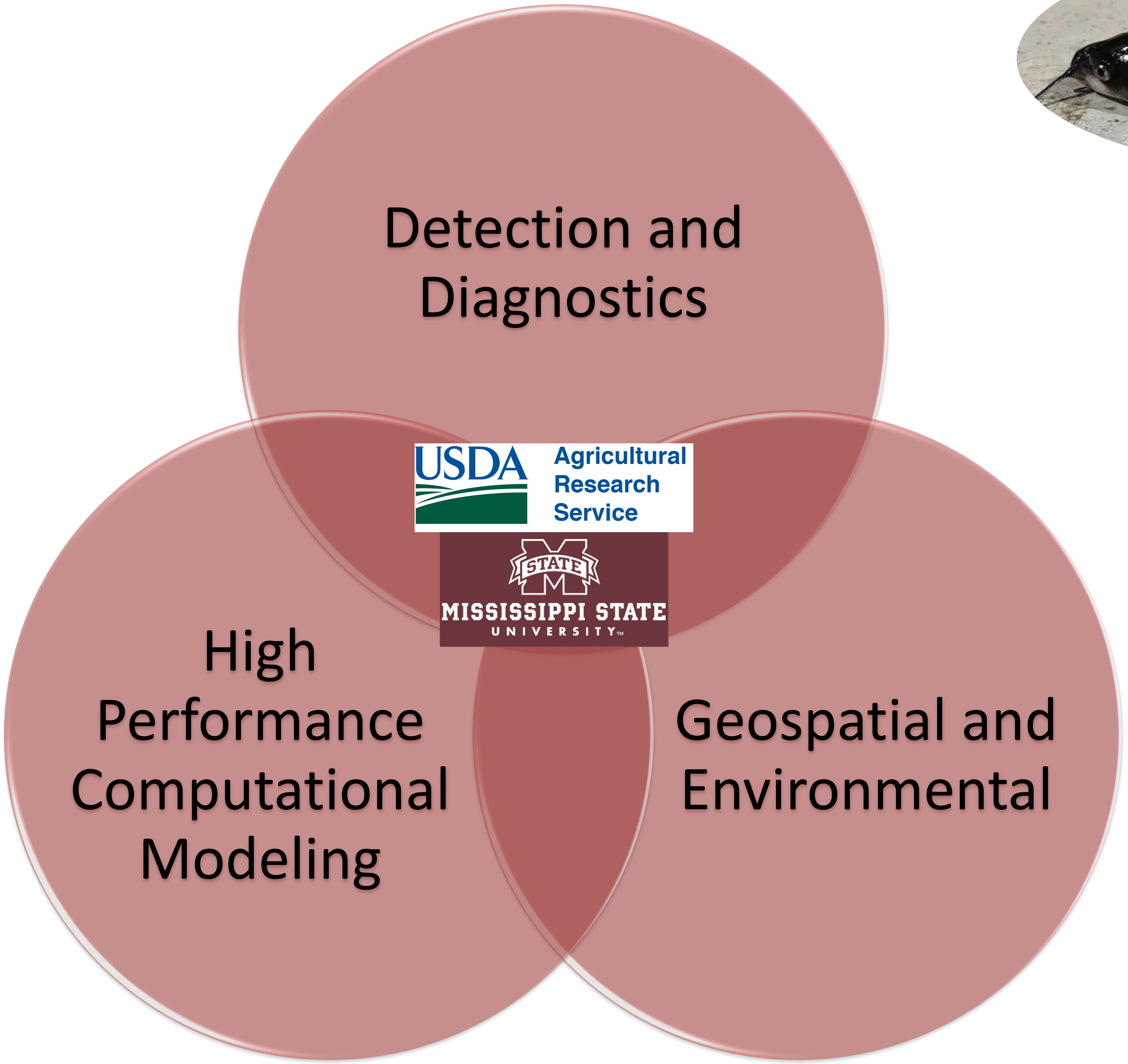
#4: Probabilistic models of bee movement using radar and environmental data

#5: Integrate movement models with robbing characteristics and triggering mechanisms to predict movements of bees and probability of robbing events

USDA ARS ATLAS HPC

- Powering research advances in biocomputing, epidemiology, and geospatial technology
- Online in 2020
- Cray CS500 Linux cluster
- 23,040 logical cores
- 101 terabytes of total RAM
- 8 NVIDIA V100 GPUs
- peak performance of 565 TeraFLOPS.




Detection and Diagnostics
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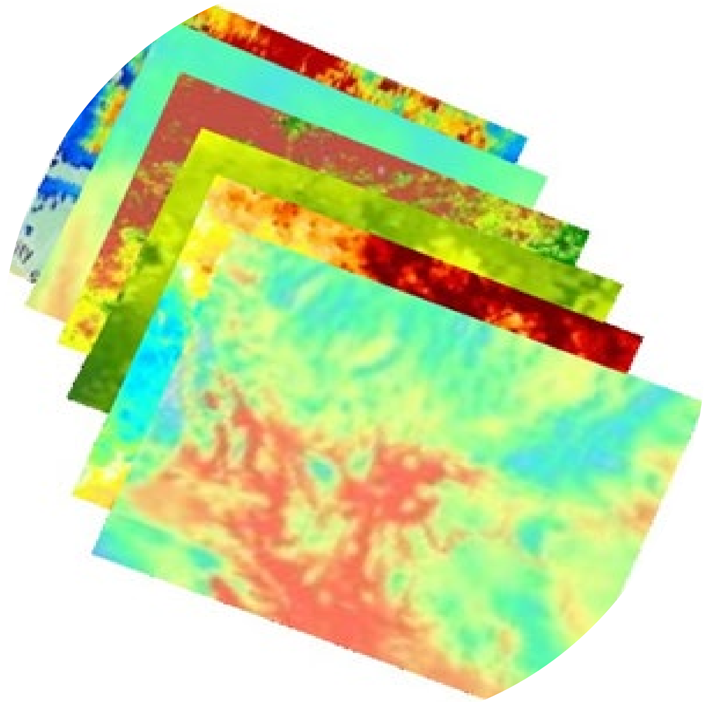

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USDA Agricultural Research Service

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