INFECTIOUS DISEASE MANAGEMENT UNDER CLIMATE CHANGE: MODELS AND APPLICATIONS

VÁLERI N. VÁSQUEZ
UNIVERSITY OF CALIFORNIA BERKELEY
JANUARY 2023

CONTEXT

CLIMATE CHANGE

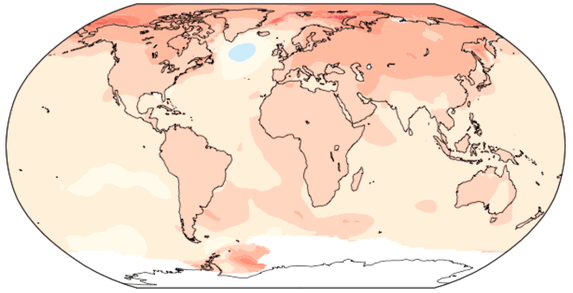
HIGHER AVERAGES

"With every increment of global warming, changes get larger in regional **mean temperature**."

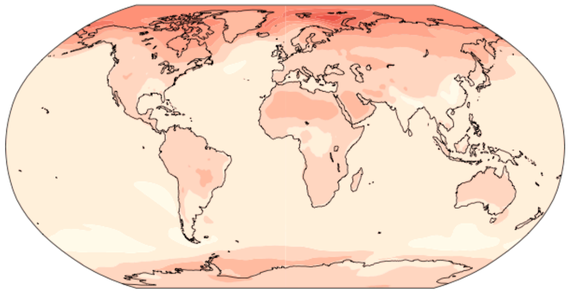
(a) Annual mean temperature change (°C) at 1°C global warming

Warming at 1°C affects all continents and is generally larger over land than over the oceans in both observations and models. Across most regions, observed and simulated patterns are consistent.

Observed change per **1°C** global warming



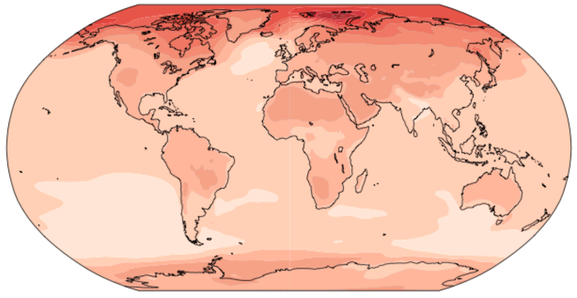
Simulated change at **1°C** global warming



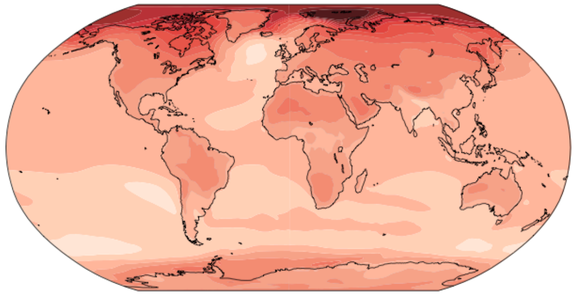
(b) Annual mean temperature change (°C) relative to 1850–1900

Across warming levels, land areas warm more than ocean areas, and the Arctic and Antarctica warm more than the tropics.

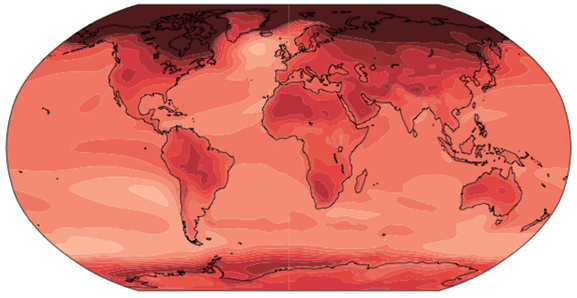
Simulated change at **1.5°C** global warming



Simulated change at **2°C** global warming



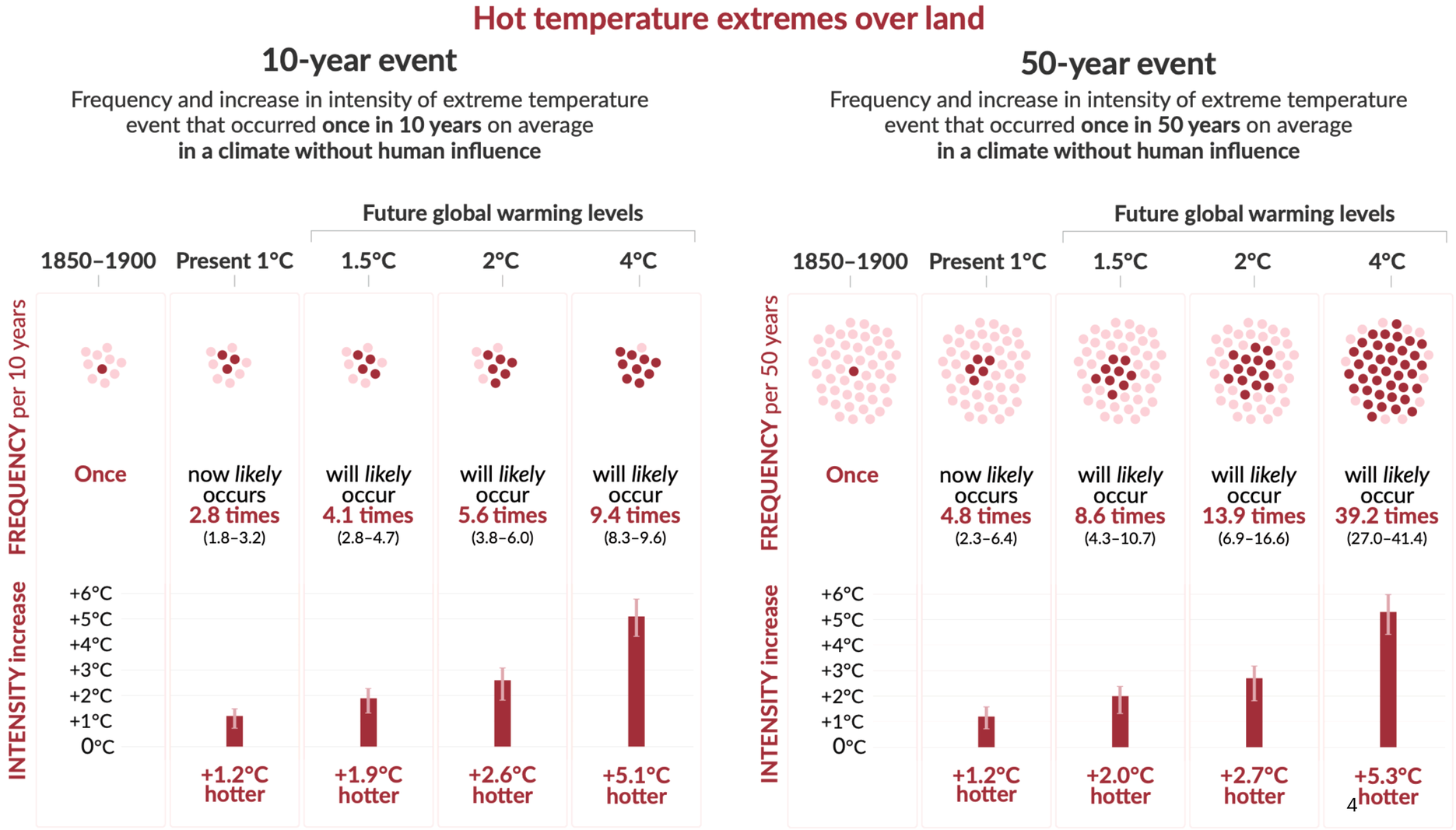
Simulated change at **4°C** global warming



CLIMATE CHANGE

GREATER EXTREMES

"Projected changes in extremes are larger in **frequency and intensity** with every additional increment of global warming."

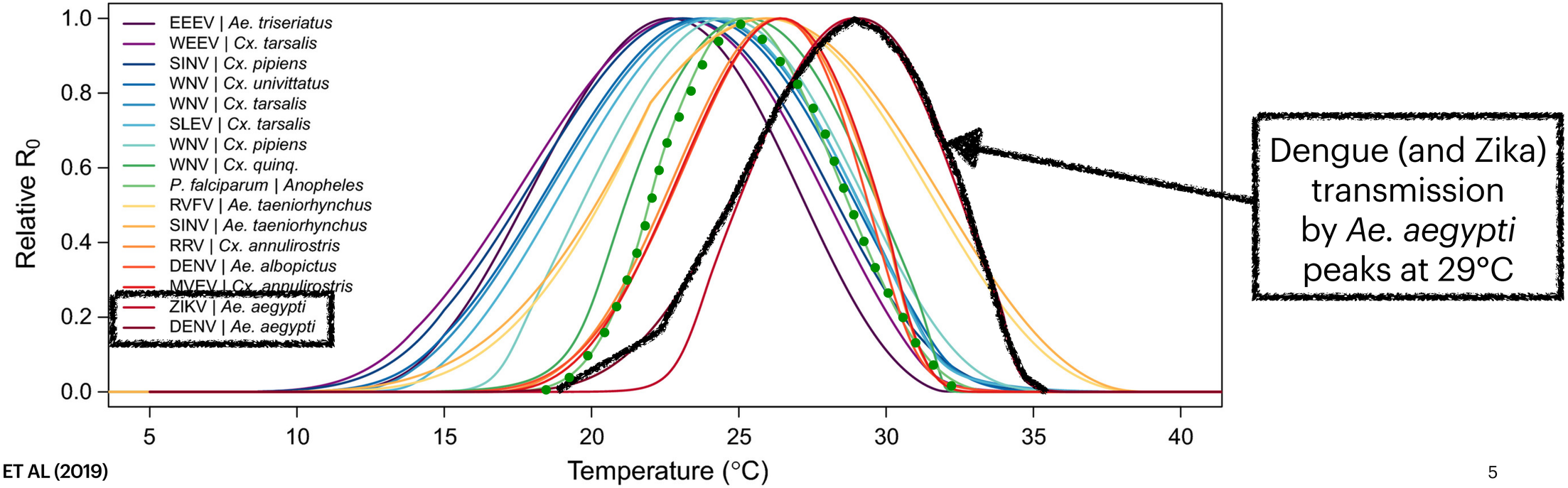


IPCC AR6

SPATIOTEMPORAL SHIFT IN DISEASE

THERMAL BIOLOGY OF VECTORS

While scientists “cannot conclusively predict changes in incidence based on temperature alone”, the thermal biology literature argues that **temperature change will promote transmission of certain diseases even as it limits transmission of others**.



MORDECAI EA ET AL (2019)

SHIFT ALSO REQUIRED FOR CONTROL

NEW CLIMATE AND DISEASE REALITIES —> NEW TOOLS NEEDED

The New York Times

Gene Drives O
Against Disea

A woman in Tanzania under a mosquito tent with a relative who was being treated for malaria. With gene drives, it may be possible to kill off a mosquito population or make the population resistant to malaria parasites. Uriel Sinai for The New York Times

nature

Explore content · About the journal · Publish with us · Subscribe

nature › news › article

NEWS | 18 April 2022

Biotech firm announces results from first US trial of genetically modified mosquitoes

Oxitec reports that its insects behaved as planned – but a larger trial is needed to learn whether they can reduce wild mosquito populations.

The New York Times

It Takes a Mosquito to Fight a Mosquito

In Australia, China and elsewhere, scientists are fighting disease-carrying mosquitoes by introducing another type, carrying just a harmless form of bacteria.

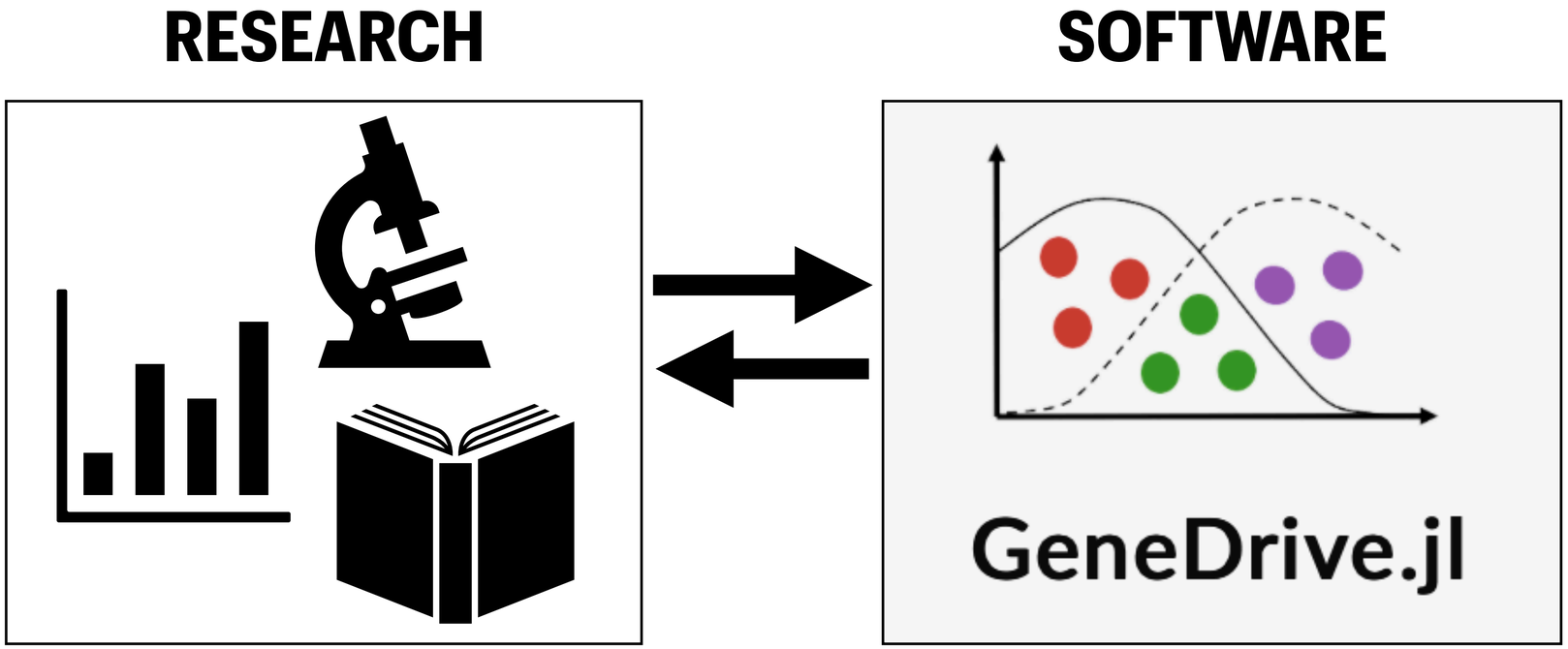
Jan. 8, 2019

Tiny Bacterium Called *Wolbachia* Could Defeat Dengue

Scientists are immunizing mosquitoes against disease with the help of a common microbe

SOFTWARE INFORMED BY SCIENCE

PHILOSOPHY OF DEVELOPMENT AND DESIGN



VÁSQUEZ ET AL, IN PREP (2023)

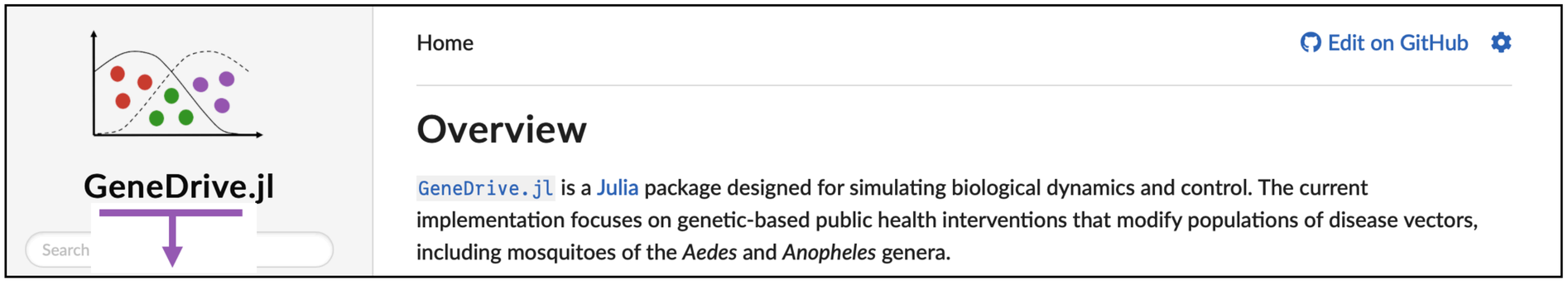

SOFTWARE

GENEDRIVE.JL

SOFTWARE INFORMED BY SCIENCE

Operational focus: genetic-based tools

- Characterize environmentally sensitive dynamics
- Define optimal policies for biocontrol



VÁSQUEZ ET AL, IN PREP (2023)

GENEDRIVE.JL

SOFTWARE INFORMED BY SCIENCE

- Open source
- Extensible and scalable
- Documentation including examples
- Collaborators welcome

README.md

GeneDrive.jl

repo status Active | Main - CI passing | codecov 63% | docs stable

Overview

`GeneDrive.jl` is a Julia package designed for simulating biological dynamics and control. The objectives of the package include:

- Provide data models that structure inputs to experimental setups and exploit the power of Julia's type system for multiple dispatch.
- Enable the creation of dynamic models that build on the `DifferentialEquations.jl` platform.
- Facilitate the formulation of decision models that employ `JuMP.jl`, the domain-specific modeling language for mathematical optimization embedded in Julia.

Installation and usage

`GeneDrive.jl` will work with Julia version 1.7 and above. Add the package with:

```
julia> ]
(v1.7) pkg> add GeneDrive
```

Begin using the package with:

```
julia> using GeneDrive
```

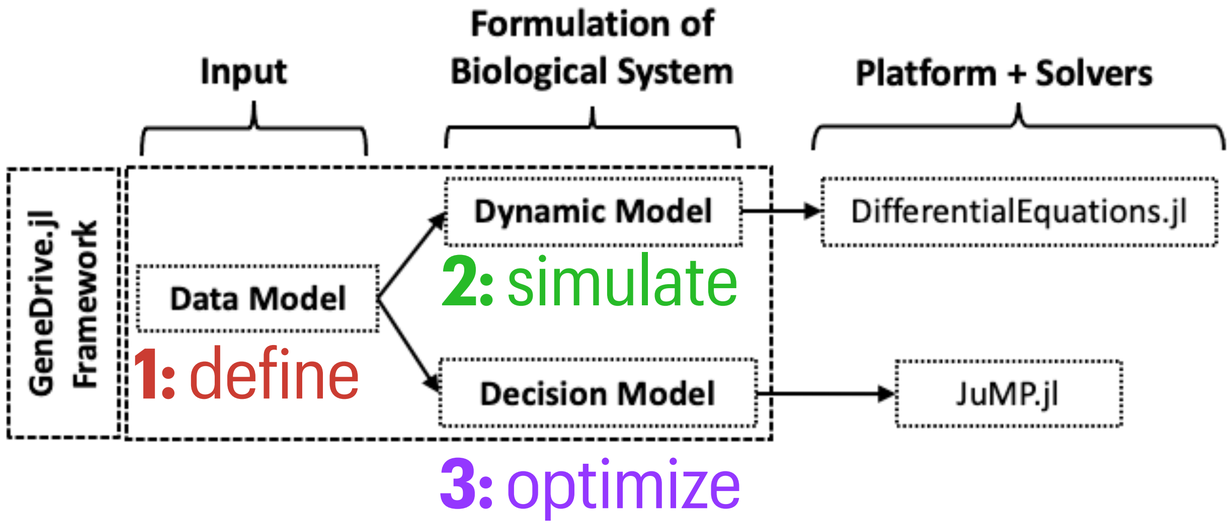
Getting started

The documentation features examples as well as more detailed descriptions of package functionalities.

VÁSQUEZ ET AL, IN PREP (2023)

GENEDRIVE.JL

A THREE-PART FRAMEWORK



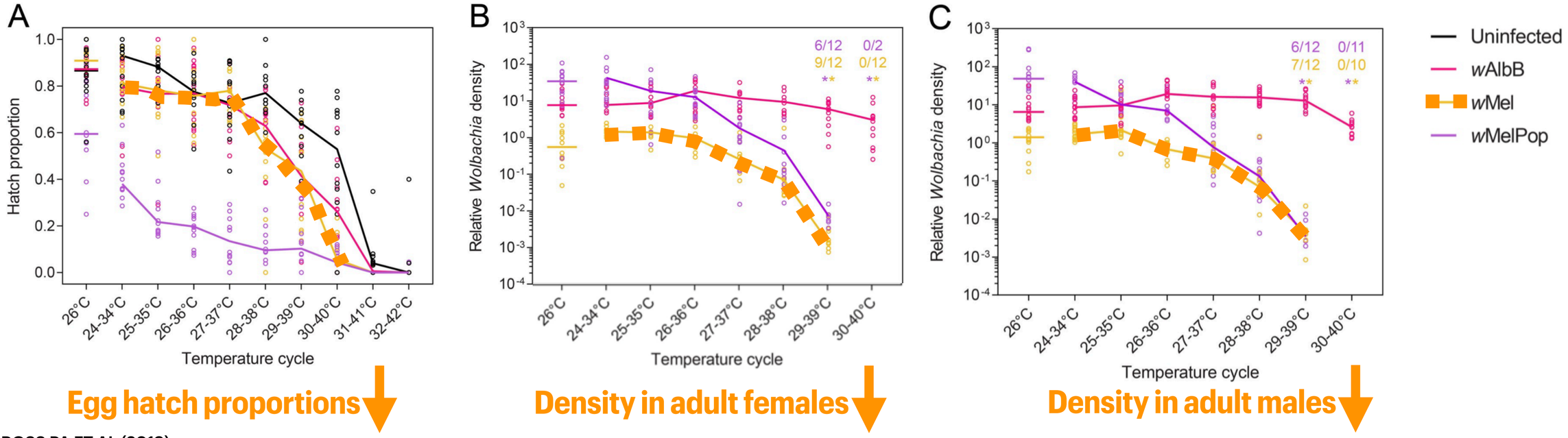
1. **Data model:** An abstraction used to define simulation inputs, store them, and dispatch methods.
2. **Dynamic model:** An ordinary differential equation formulation of the biological system.
3. **Decision model:** A discretized implementation of the biological system as a nonlinear mathematical program.

RESEARCH AREA #1

TECHNOLOGICAL: WHAT TOOLS ARE (CLIMATE) APPROPRIATE?

THERMAL BIOLOGY OF GENETIC-BASED INTERVENTION: WOLBACHIA (*w*MEL) → Most widely deployed bacterial strain

- *Wolbachia* infection: maternally inherited, and pathogen blocking.
- Key phenotype enabling use as a public health tool is weakened by cyclical heat stress.
- High temperatures can **cause the infection to fall out of the population entirely past 35°C**

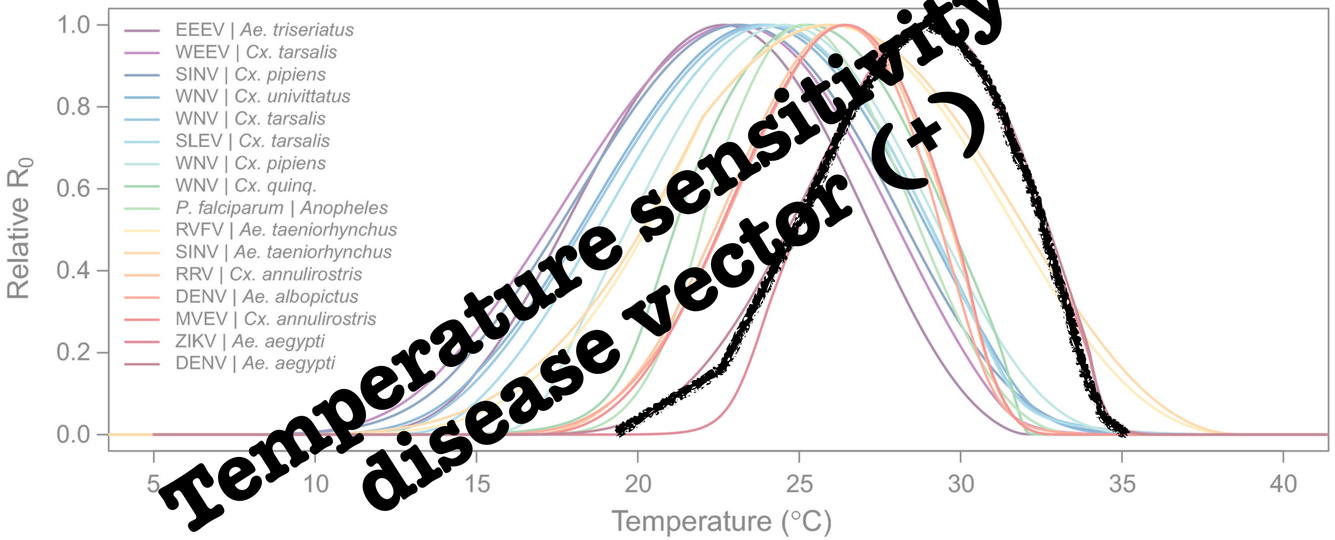


Egg hatch proportions ↓ **Density in adult females** ↓ **Density in adult males** ↓

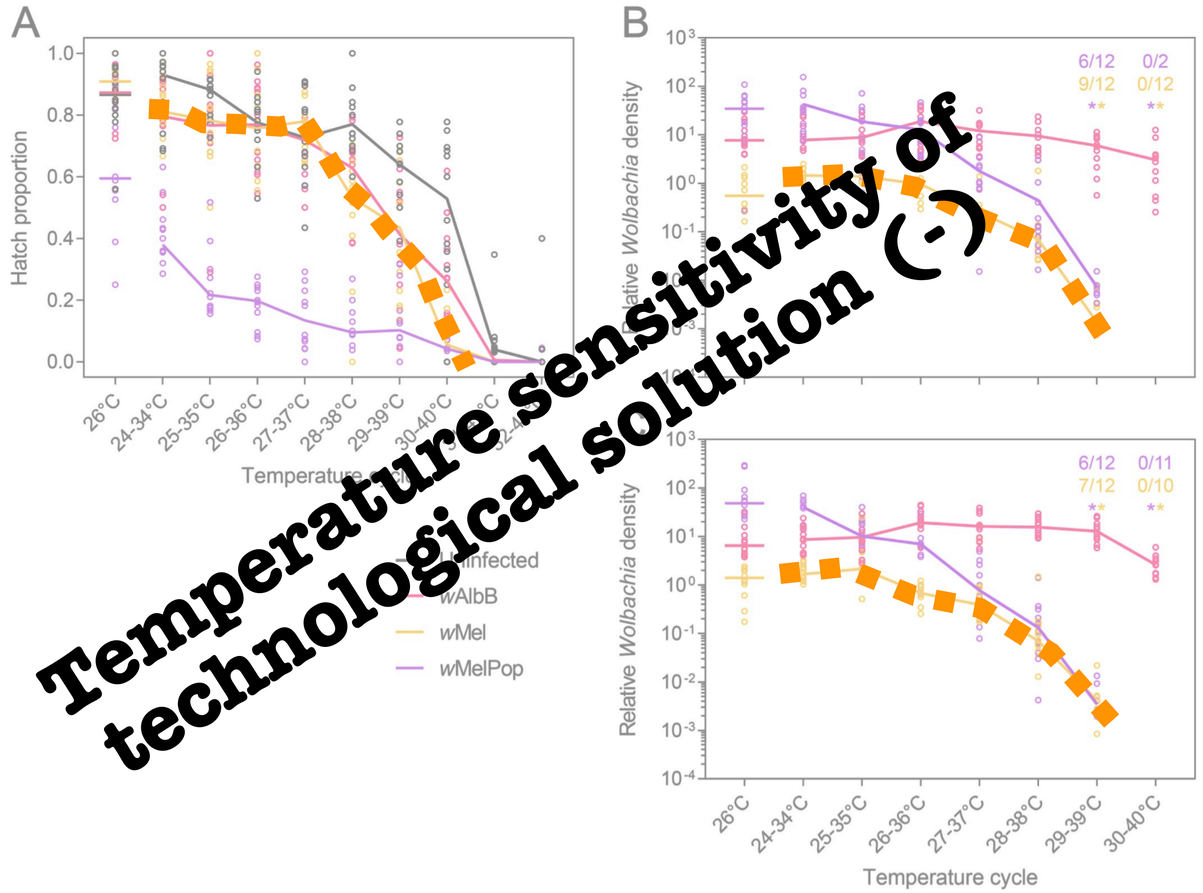
ROSS PA ET AL (2019)

TECHNOLOGICAL: WHAT TOOLS ARE (CLIMATE) APPROPRIATE?

THERMAL BIOLOGY OF GENETIC-BASED INTERVENTION: WOLBACHIA (*w*MEL)



Temperature sensitivity of disease vector (+)



Temperature sensitivity of technological solution (-)

MORDECAI EA ET AL (2019)

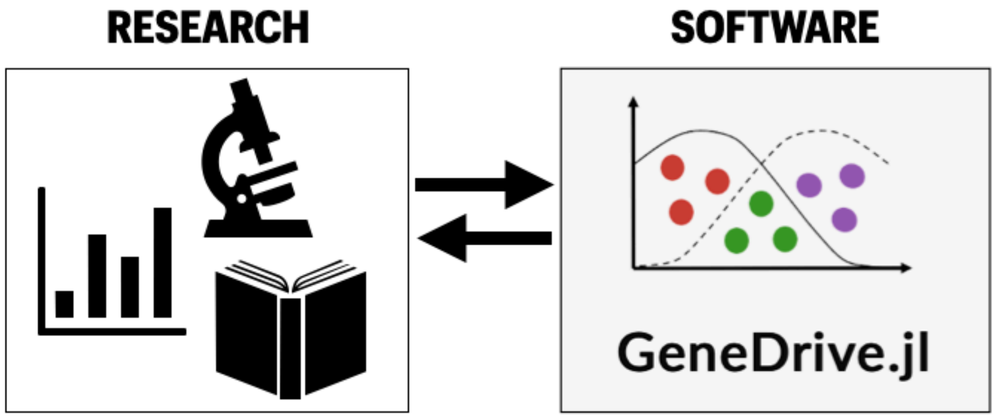
ROSS PA ET AL (2019)

EVALUATING WHETHER TOOLS ARE (CLIMATE) APPROPRIATE

THE CASE FOR SOFTWARE

- Empirical research is essential: both laboratory and field studies furnish fundamental insights.
- To evaluate findings in the **necessary context (e.g., future climate realities)**, models are required.
- Models facilitate hypothesis testing:
  - ❖ **Explore uncertainties** in empirical data
  - ❖ **Extrapolate** to include new scenarios

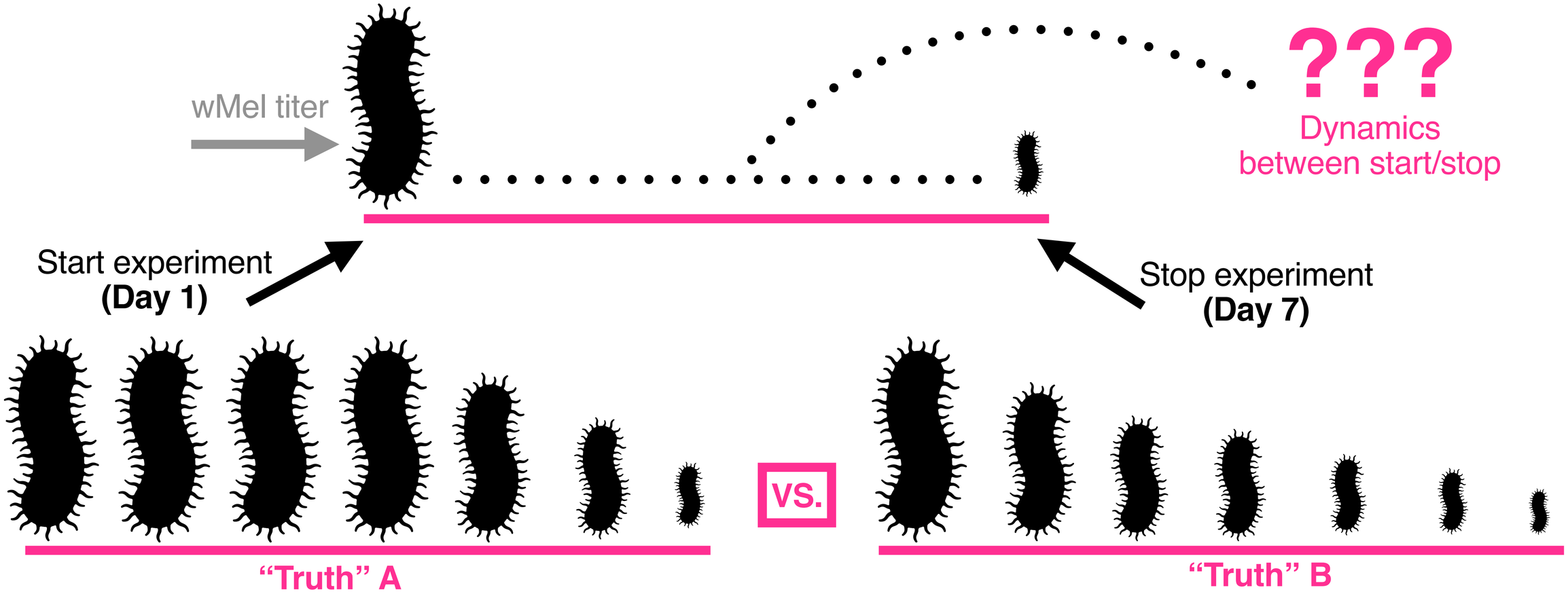
Formalize in software for "modular" modifications, scientific replicability



VÁSQUEZ ET AL, IN PREP (2023)

REQUIREMENT: EXPLORE UNCERTAINTIES

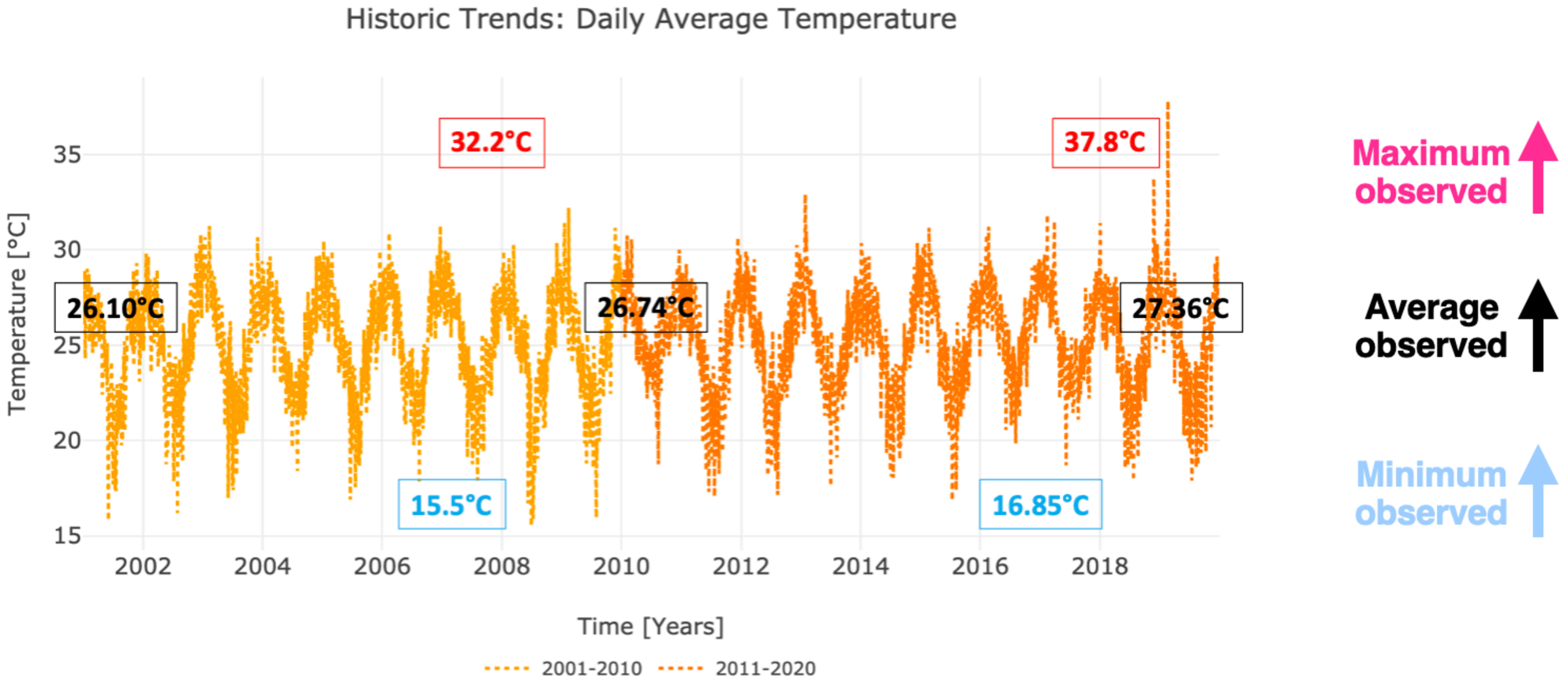
SOFTWARE TO ELUCIDATE THE TEMPORAL RESOLUTION OF TEMPERATURE EFFECTS



VÁSQUEZ ET AL, IN REVISION (2023)

REQUIREMENT: EXTRAPOLATE TO NEW SCENARIOS

SOFTWARE TO EXAMINE INTERVENTION EFFICACY UNDER FUTURE TEMPERATURES



VÁSQUEZ ET AL, IN REVISION (2023)

SOFTWARE DESIGNED TO MEET RESEARCH REQUIREMENTS

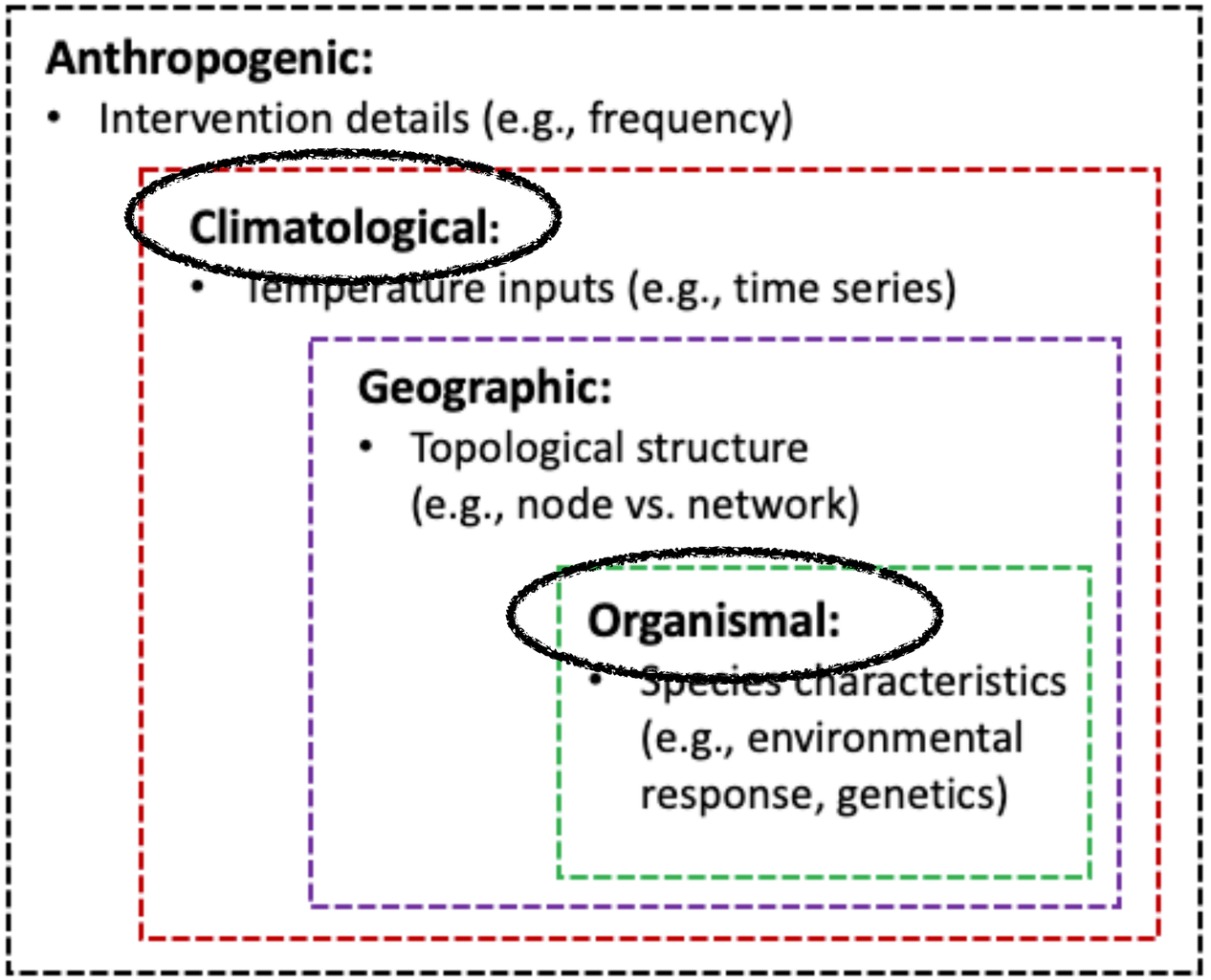
GENEDRIVE.JL: THE DATA MODEL

In principle:

- Straightforward to change or add new information as it becomes known
- Composability enables co-evolution with scientific discovery

In practice (for this research):

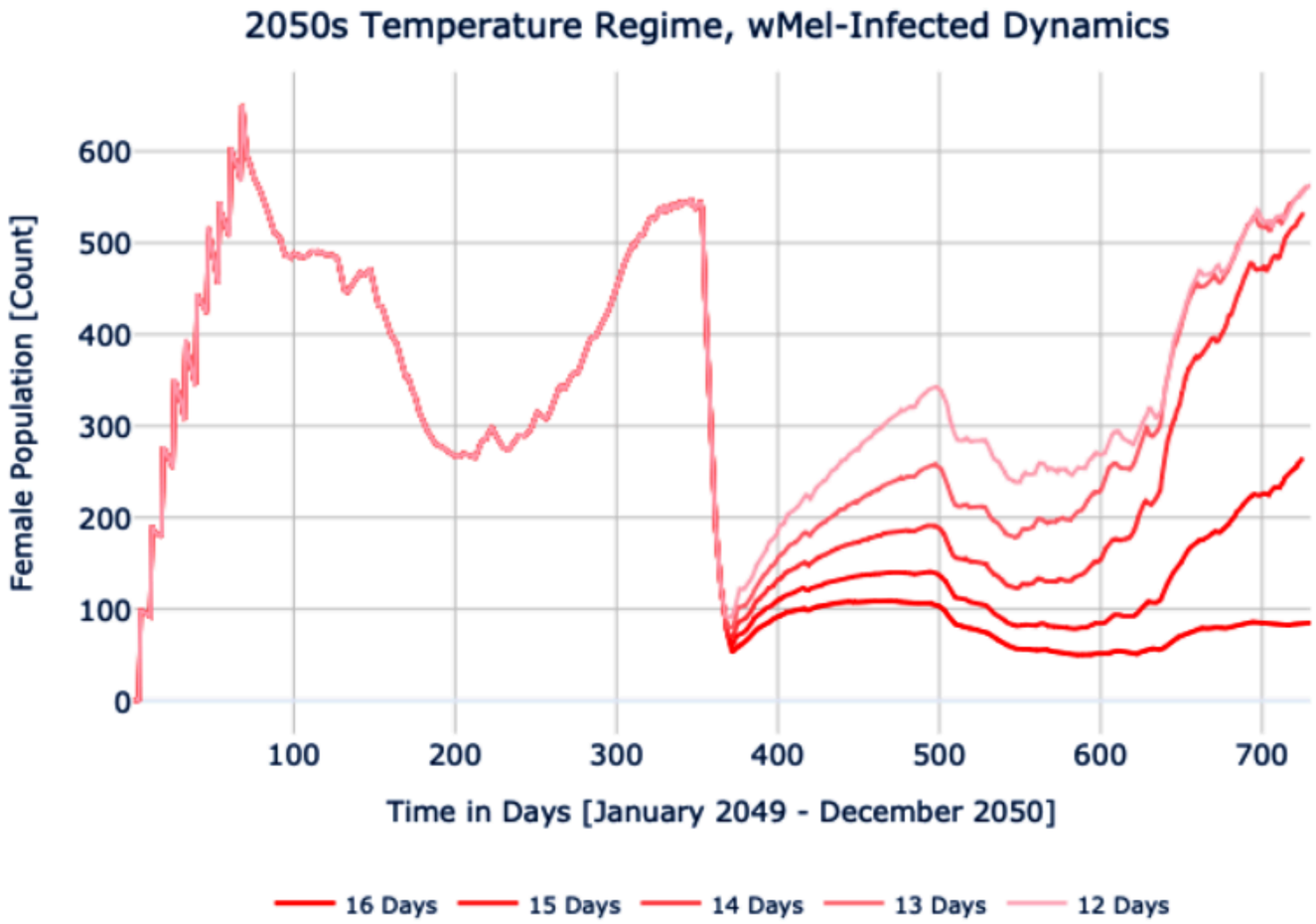
- Alternative functional forms: Wolbachia's thermal sensitivity, distinct from its *Ae. aegypti* host
- Alternative data inputs: Temperature time series for 2030s, 2050s, etc. (averages and heatwaves)



VÁSQUEZ ET AL, IN PREP (2023)

FINDING: WOLBACHIA IS ROBUST TO FUTURE CLIMATES

THERMAL BIOLOGY OF GENETIC-BASED INTERVENTION: WOLBACHIA (*w*MEL)



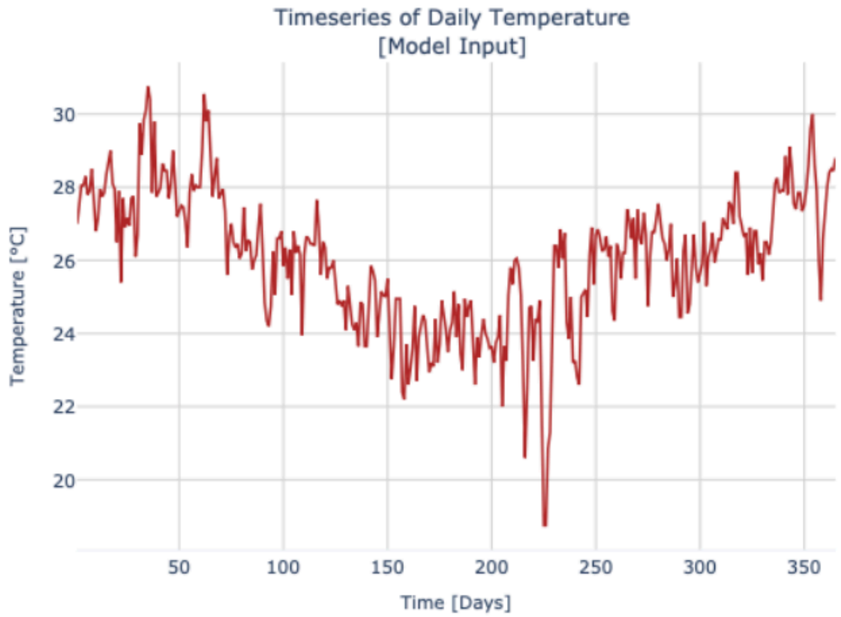
VÁSQUEZ ET AL, IN REVISION (2023)

RESEARCH AREA #2

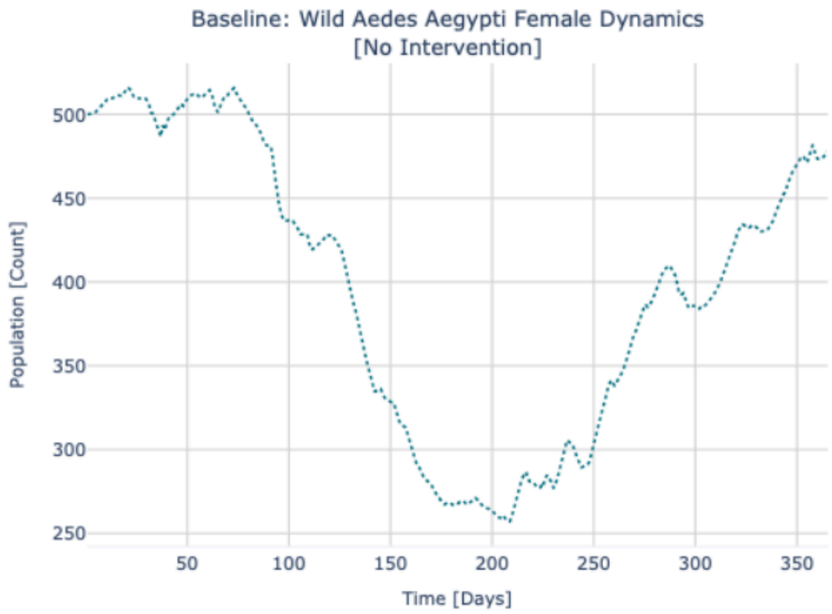
STRATEGIC: WHAT IS THE "BEST" ALLOCATION OF TOOLS?

DEFINING "BEST": THE ECOLOGICAL CONSIDERATIONS

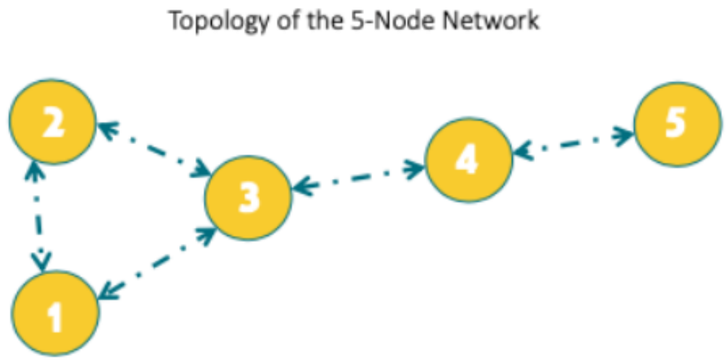
Location-specific factors are changing with shifting climates and land use practices (e.g., urbanization).



Seasonal, daily temperatures in the location of interest



Species lifecycle and adaptations in that location



Geographic connectedness, spatial distribution

VÁSQUEZ ET AL, IN REVIEW (2023)

STRATEGIC: WHAT IS THE "BEST" ALLOCATION OF TOOLS?

DEFINING "BEST": THE HUMAN HEALTH AND ECONOMIC CONSIDERATIONS

- The efficacy of a given public health intervention translates to lives saved and illness prevented.
- Efficiency gains also equate to cost reductions: deployment demands resources
  - ❖ Potentially fewer or more infrequent trips to the field (labor cost)
  - ❖ Smaller numbers of organisms released (material cost)
- Community comfort factor?

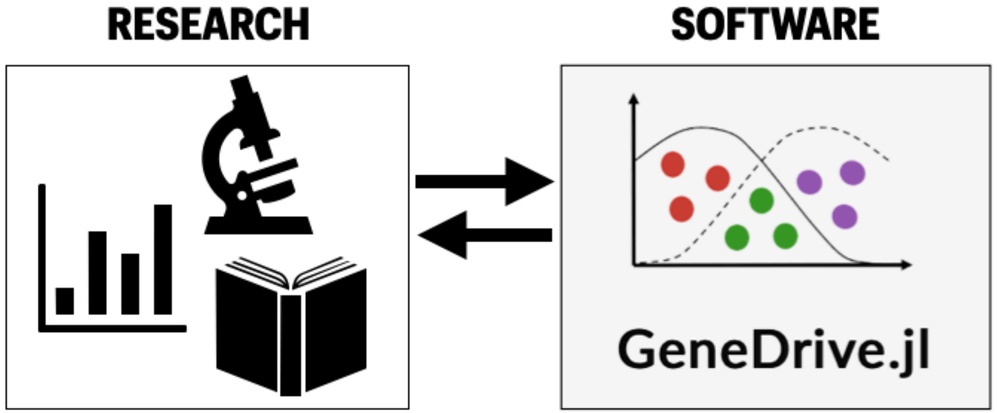
VÁSQUEZ ET AL, IN REVIEW (2023)

EVALUATING WHAT STRATEGY IS "BEST"

THE CASE FOR SOFTWARE

- **Again:** Empirical research is essential; both laboratory and field studies furnish fundamental insights.
- But models help evaluate findings in the **necessary context (e.g., alternative definitions of "best")**.
- Models facilitate hypothesis testing:
  - ❖ **Explore differences** in goals (objectives)
  - ❖ **Extrapolate** to include new scenarios

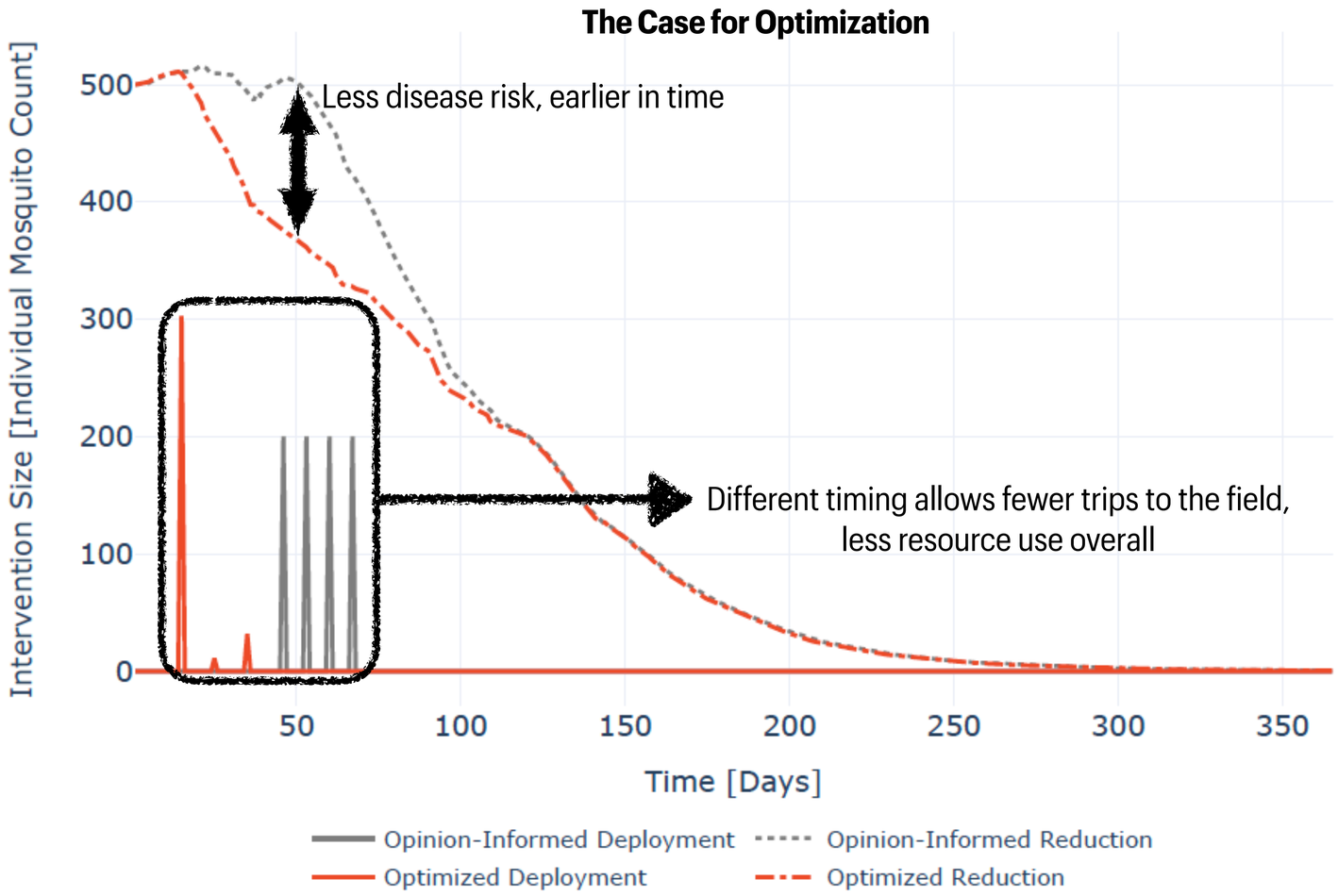
Coherence within a single framework



REQUIREMENT: IMPROVE ON THE STATE OF THE ART

SOFTWARE TO MAXIMIZE AND ITERATE OBJECTIVES, CONSIDERING RELEVANT DETAILS

- Presently, interventions designed based on the results of field work & expert opinion.
- Seeking:
  - ❖ A cheaper, more reproducible way to strategize
  - ❖ Ability to update when details change (as they do)
- Answer: optimization?



VÁSQUEZ ET AL, IN REVIEW (2023)

SOFTWARE DESIGNED TO MEET RESEARCH REQUIREMENTS

GENEDRIVE.JL: THE DECISION MODEL

Objective function: Various. Here, minimize wild vector (females, *F*) using minimal releases (genetically modified, *c_ghat*)

Equality constraints: Lifecycle dynamics

Parameterization: Ecological and genetic details

Inequality constraints: Operational restrictions on deployments of *c_ghat*

$$\min_{c_{\hat{g},t}} \quad J\left(F_{n,g,t}, \alpha c_{\hat{g},t}\right)$$

$$E_{g,t,i} = E_{g,t,i-1} - E_{g,t,i}(\mu_E + q_E i_E)$$

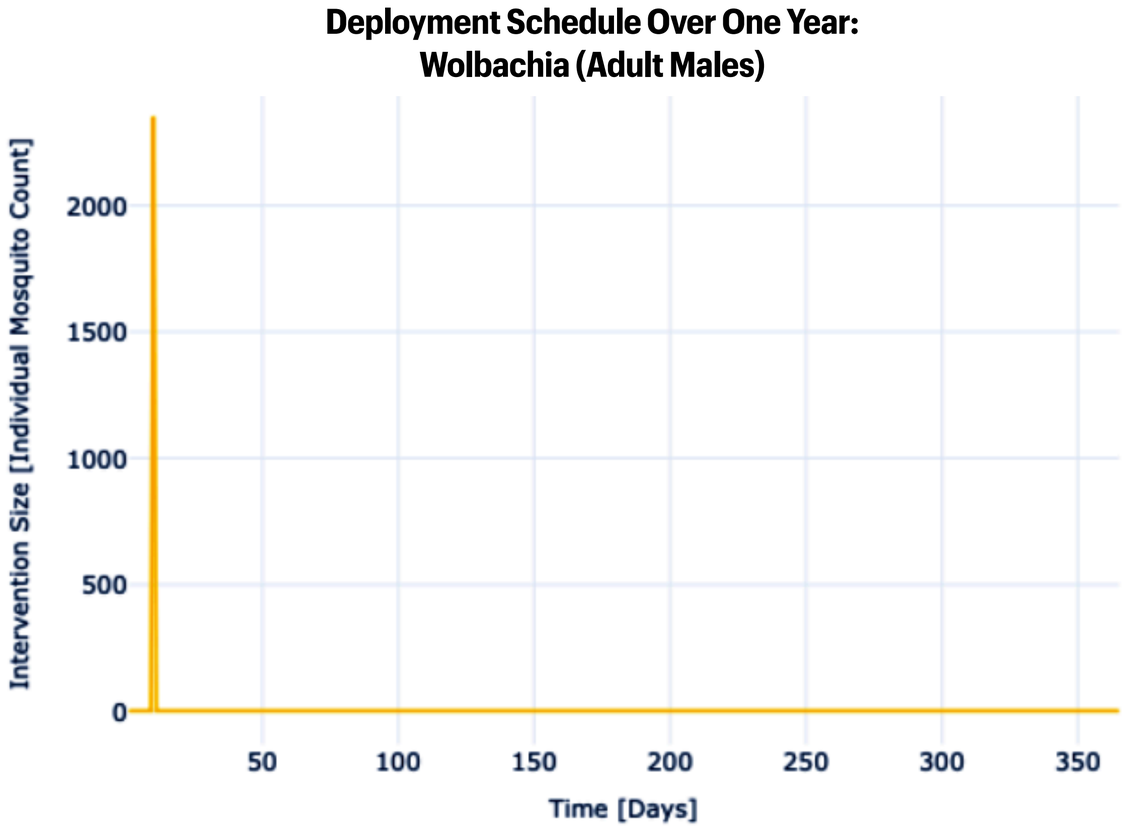
$$c_{\hat{g},t} \leq R_{n,t} D_{max}^{day} \quad \forall t \in \mathcal{T}_d,$$

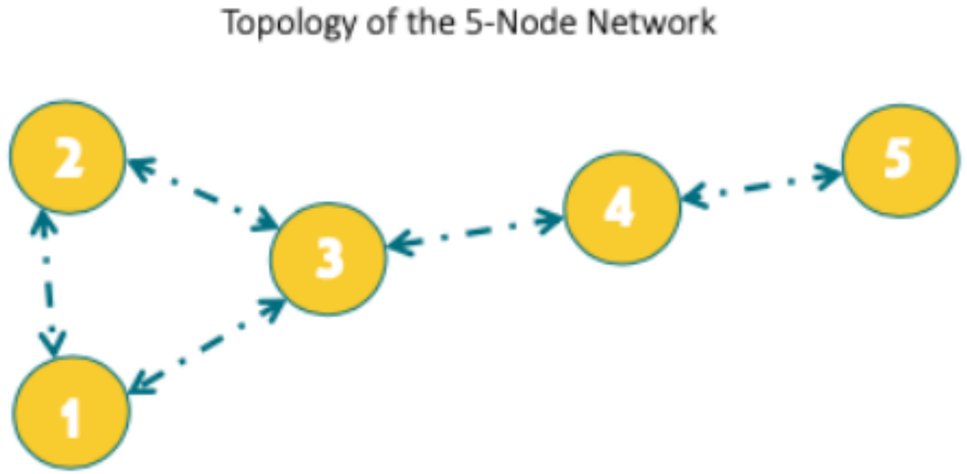
$$c_{\hat{g},t} \geq R_{n,t} D_{min}^{day} \quad \forall t \in \mathcal{T}_d,$$

$$\sum_{t \in \mathcal{T}_d} c_{\hat{g},t} \leq D_{max}^{trial}$$

FINDING: CAPABLE OF EXPLORING DIFFERENT OBJECTIVES

RISK REDUCTION ACROSS ENTIRE REGION (NETWORK) OF INTEREST





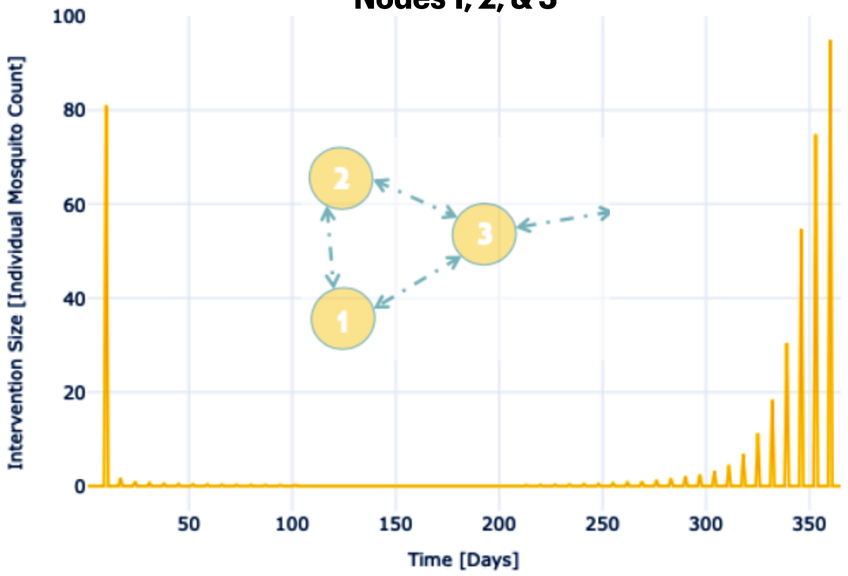
VÁSQUEZ ET AL, IN REVIEW (2023)

FINDING: CAPABLE OF EXPLORING DIFFERENT OBJECTIVES

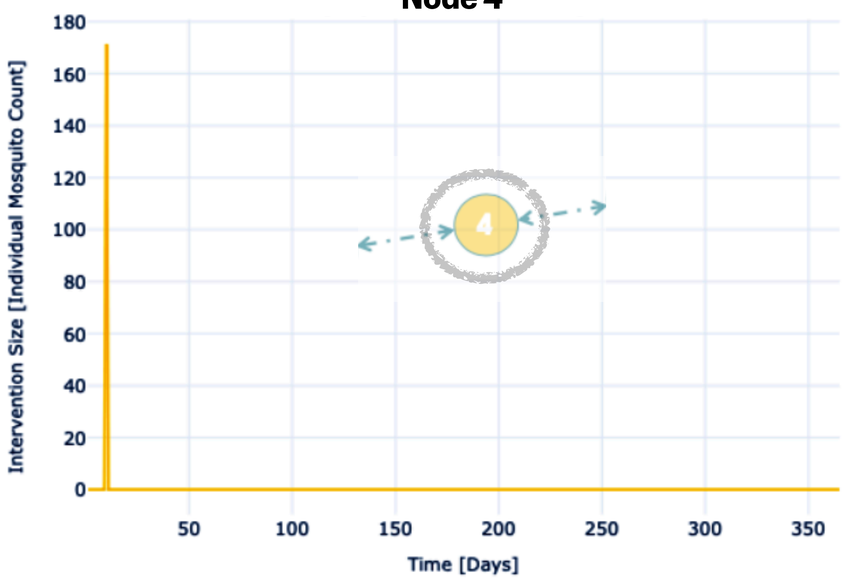
RISK REDUCTION PRIORITIZING SINGLE LOCATION OF INTEREST IN A REGION (NETWORK)

Release policy in each area of the network is dependent on its connectivity to the node of interest.

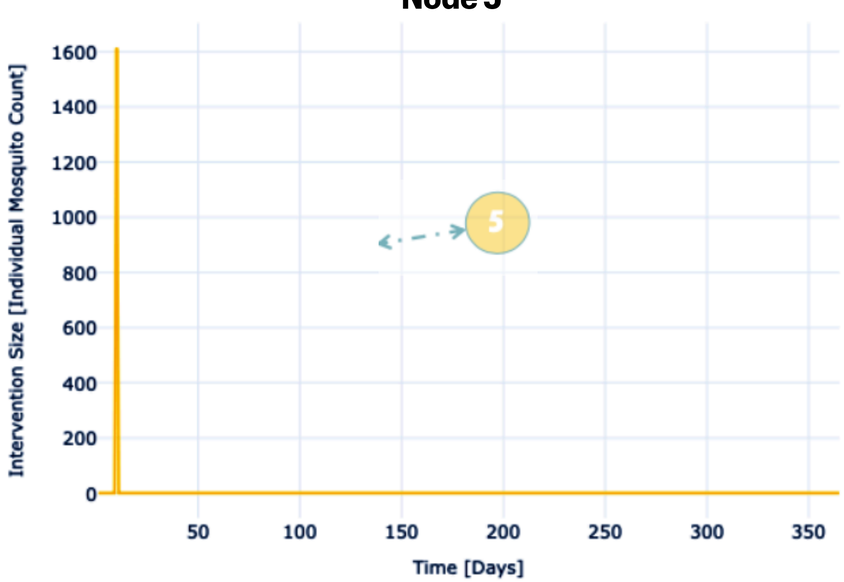
Deployment Schedule Over One Year: Nodes 1, 2, & 3

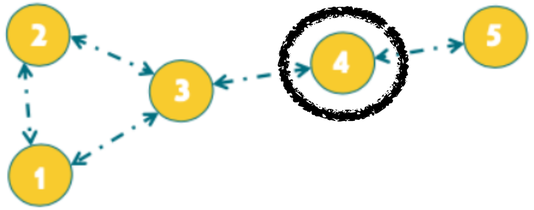


Deployment Schedule Over One Year: Node 4



Deployment Schedule Over One Year: Node 5





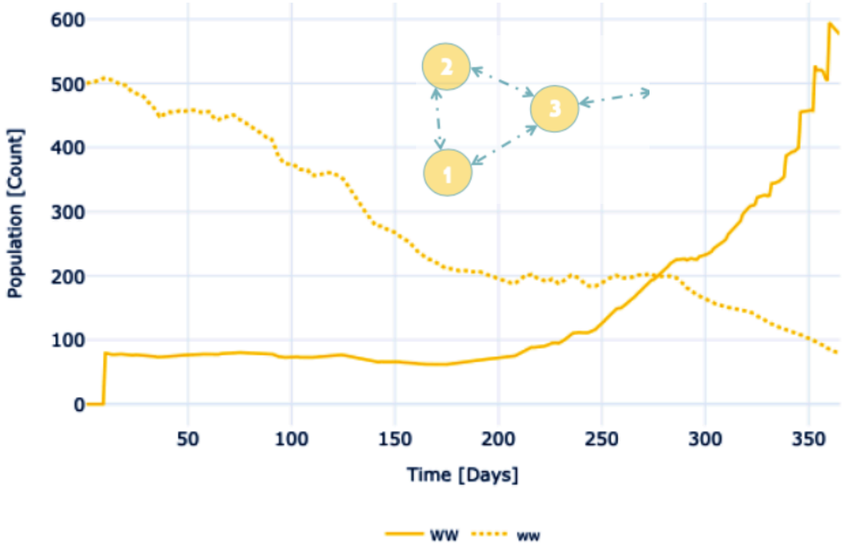
VÁSQUEZ ET AL, IN REVIEW (2023)

FINDING: CAPABLE OF EXPLORING DIFFERENT OBJECTIVES

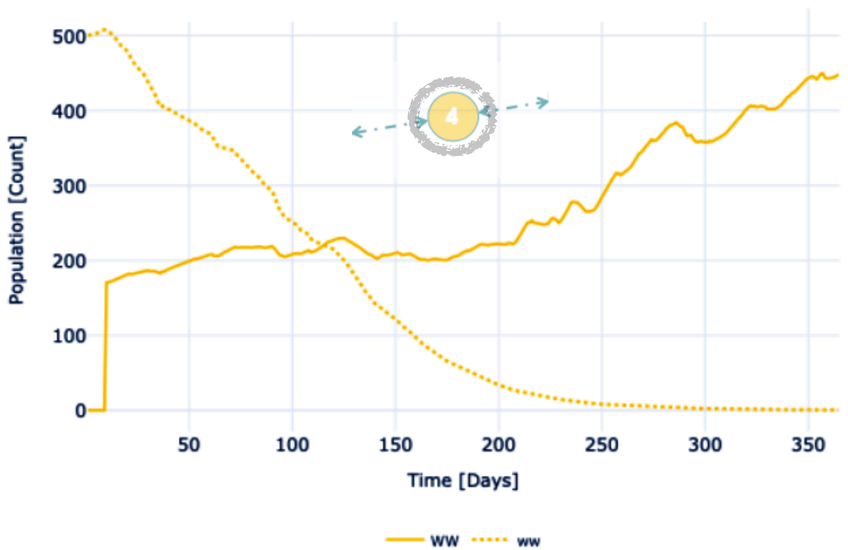
RISK REDUCTION PRIORITIZING SINGLE LOCATION OF INTEREST IN A REGION (NETWORK)

Release policy in each area of the network is dependent on its connectivity to the node of interest.

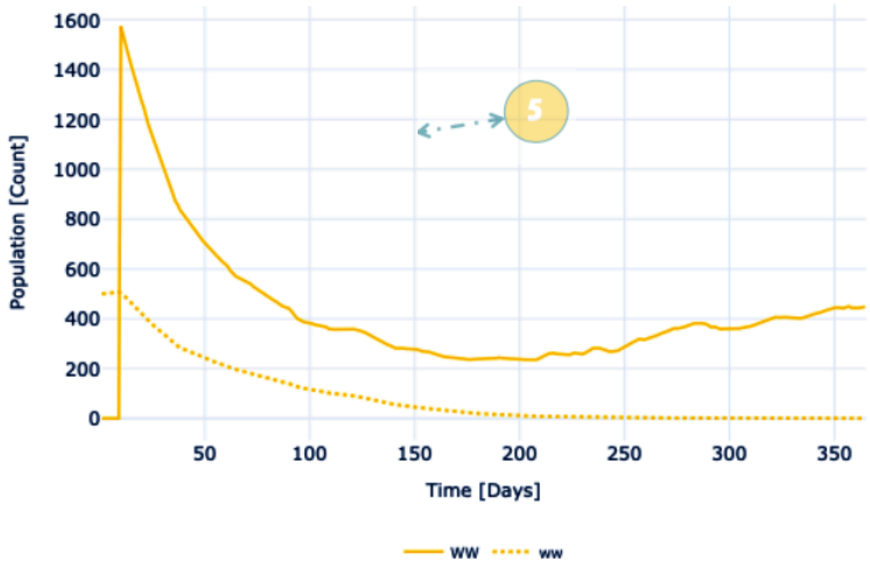
Corresponding Change in Disease Vector Over One Year: Nodes 1, 2, & 3

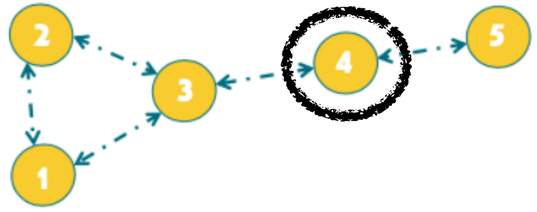


Corresponding Change in Disease Vector Over One Year: Node 4



Corresponding Change in Disease Vector Over One Year: Node 5

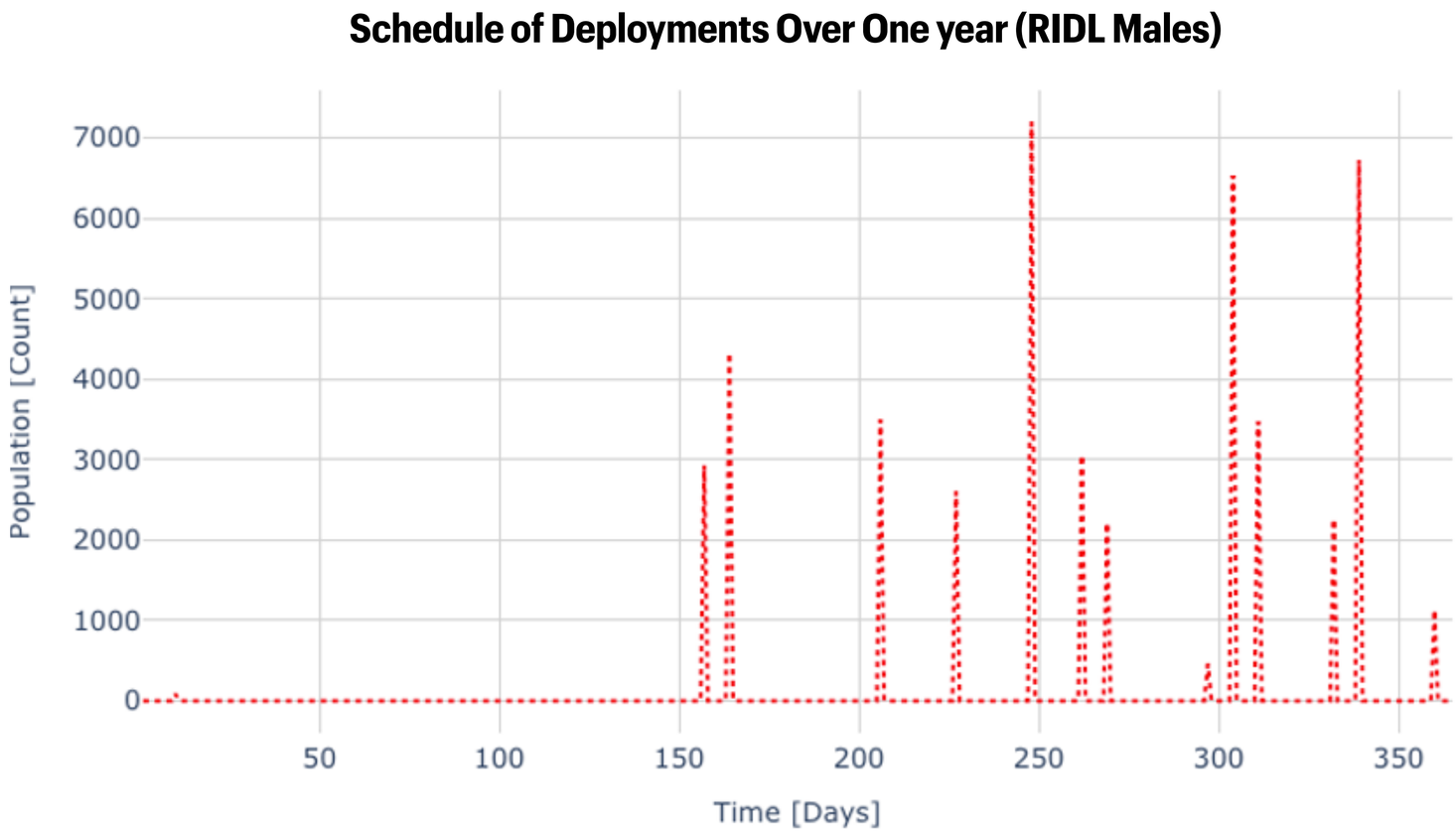




VÁSQUEZ ET AL, IN REVIEW (2023)

FINDING: CAPABLE OF EXTRAPOLATING TO NEW SCENARIOS

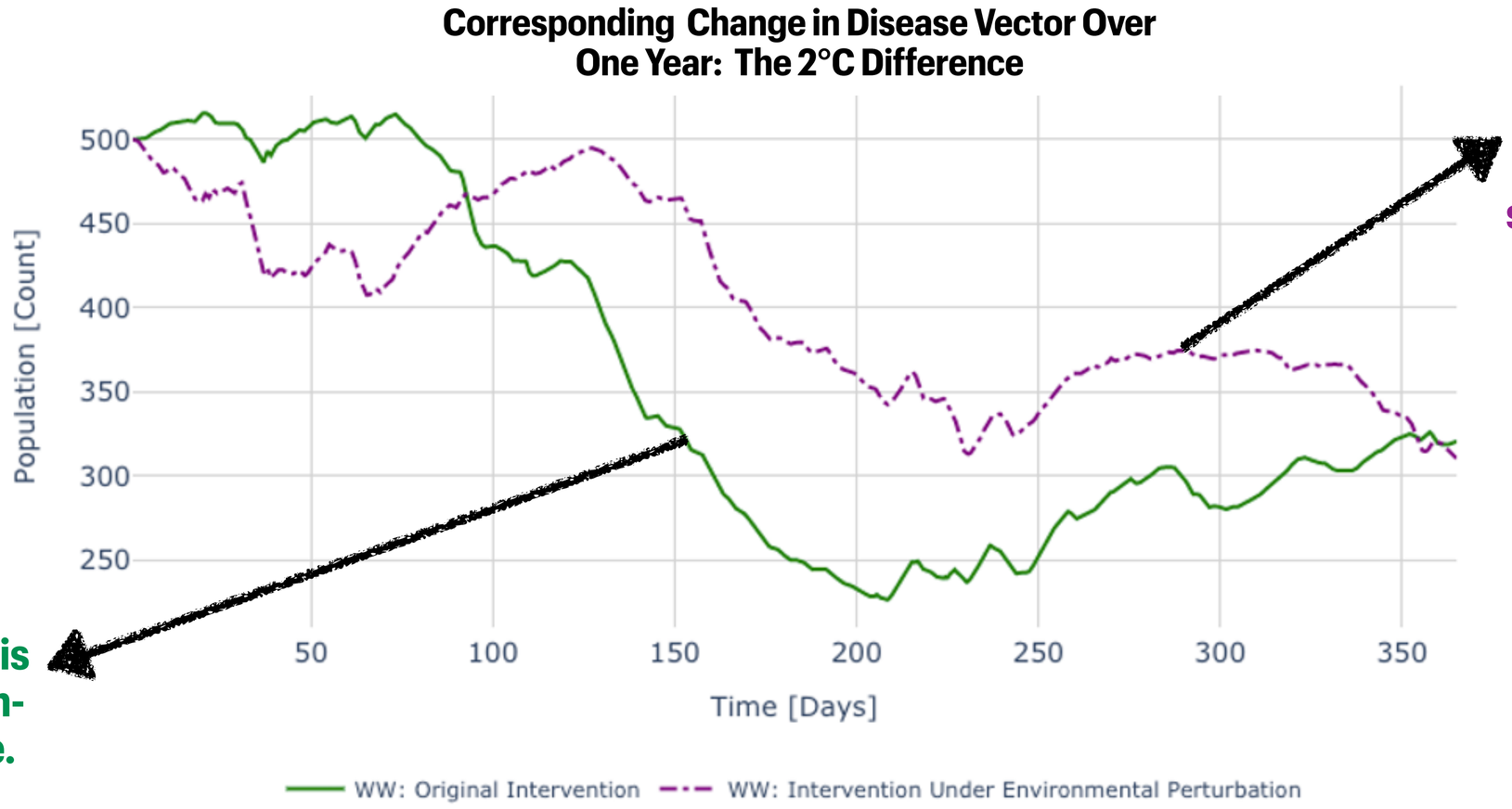
ALTERED STRATEGY TO ACCOUNT FOR CHANGING CLIMATE



VÁSQUEZ ET AL, IN PREP (2023)

FINDING: CAPABLE OF EXTRAPOLATING TO NEW SCENARIOS

ALTERED STRATEGY TO ACCOUNT FOR CHANGING CLIMATE



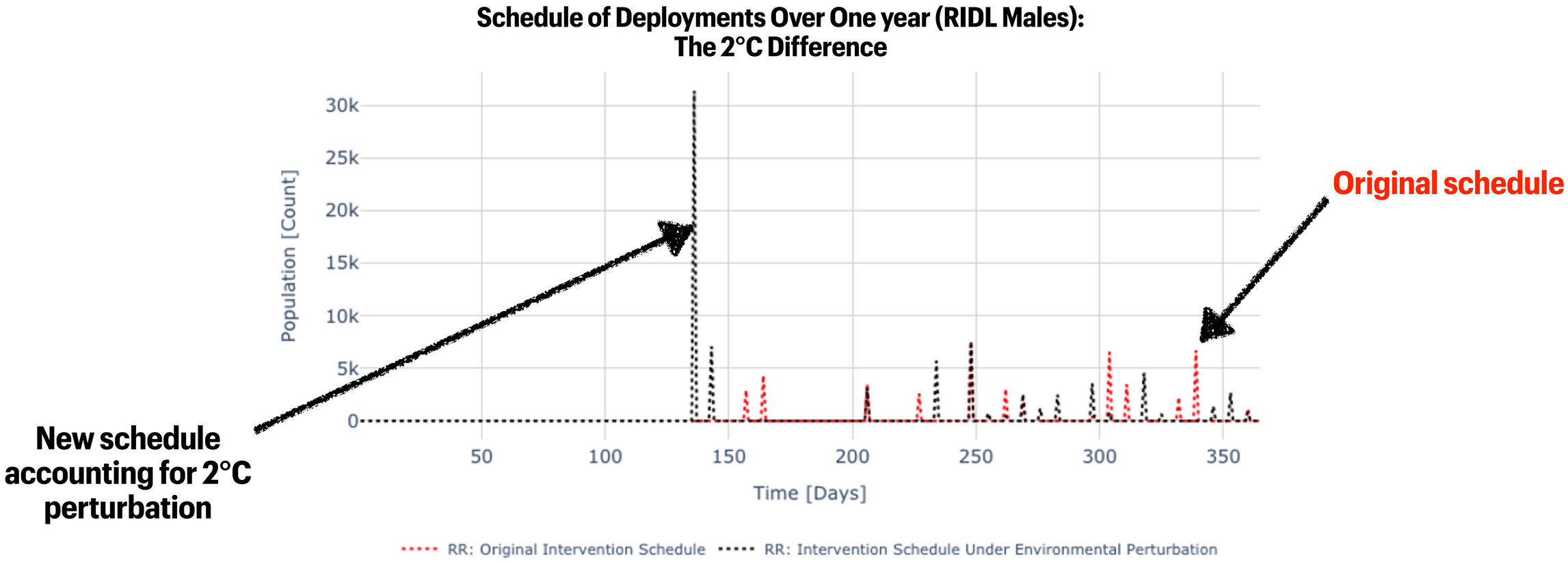
Result when annual average temperature increases 2°C, but same strategy is used.

Result when strategy is optimized for location-specific temperature.

VÁSQUEZ ET AL, IN PREP (2023)

FINDING: CAPABLE OF EXTRAPOLATING TO NEW SCENARIOS

ALTERED STRATEGY TO ACCOUNT FOR CHANGING CLIMATE



VÁSQUEZ ET AL, IN PREP (2023)

CURRENT FUNDING:

- MICROSOFT RESEARCH PHD FELLOWSHIP

COLLABORATORS:

- LARA M. KUEPPERS, UC BERKELEY
- GORDANA RAŠIĆ, QUEENSLAND INSTITUTE OF MEDICAL RESEARCH (QIMR)
- JOHN M. MARSHALL, UC BERKELEY
- DAVID ANTHOFF, UC BERKELEY
- MICHAEL REDDY, MICROSOFT RESEARCH - HEALTH FUTURES

THANK YOU