Simulating nitisinone based intervention on mosquito populations

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Introduction

Recent breakthroughs have demonstrated the potential of the drug nitisinone (NTBC) as a novel vector-targeted insecticide, where vertebrate blood becomes lethal to mosquitoes after drug exposure [2, 3, 4]. This paradigm-shifting approach can be deployed through various methods, including human inoculation, topical skin application, or environmental spraying. The critical question remains: which delivery strategy is most effective for mosquito population control? In this study, we employ agent-based modeling (ABM) by extending our simulation software, COMORBUSS, to quantitatively evaluate and compare the efficacy of these distinct NTBC delivery methods.

COMORBUSS

COMORBUSS [1] is a biosocial stochastic agent-based community model, built from chosen city data coupled to biological models for disease propagation and progression. The simulations follow individual infections, measuring how much the simulated protocols reduce infection in each basic component of the community (e.g. schools, markets, home, workplaces). Such detailed analysis targeted at particular cities can produce recommendations that respect the limitations and needs of specific communities. On this work we are expanding COMORBUSS to simulate propagation of diseases by vectors (e.g. dengue, malaria, oropouche).

Mosquito Model

Mosquito Population Dynamics: We used an agent-based model for female mosquito population with stochastic reproduction and mortality. Each mosquito has individual attributes including age, position, feeding status, and infection state. The population follows a birth-death process where reproduction occurs probabilistically at rate r_m (reproduction probability per mosquito per day), with new mosquitoes replacing deceased ones up to a maximum carrying capacity. Mosquitoes lifespans follow a exponential distribution with mean τ_{life}.

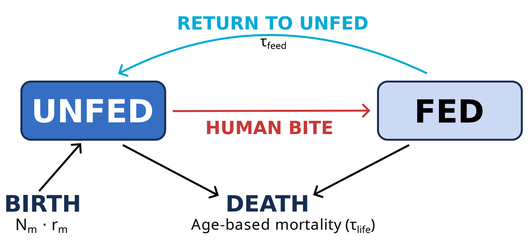

Figure 1. Mosquito feeding cycle

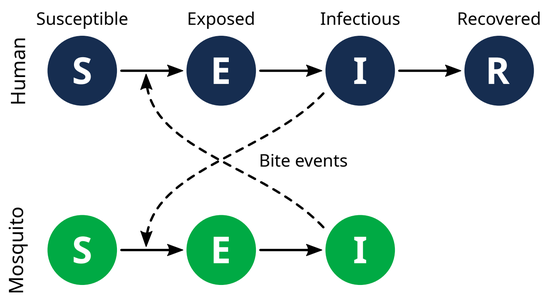

Figure 2. Infection diagram

Feeding Cycle and Disease Transmission: Mosquitoes follow a discrete feeding cycle (Figure 1) where unfed mosquitoes seek blood meals from humans within the same buildings or geographic proximity with bite probability p_{bite}. After feeding, mosquitoes enter a refractory period τ_{feed} during which they cannot bite again. Disease transmission (Figure 2) occurs bidirectionally with probabilities p_{h2m} (human-to-mosquito) and p_{m2h} (mosquito-to-human). The model incorporates an extrinsic incubation periods τ_{incub}.

Spatial Dynamics and Human-Vector Interactions: Mosquito movement follows configurable models including random walk with average speed v_{mosq} within bounded geographic areas derived from real OpenStreetMap building data. Human-mosquito encounters occur through two mechanisms: building-based interactions when mosquitoes and humans are located in the same structure and proximity interactions within radius r_{env} with encounter probability p_{env} for agents in outdoor spaces.

References

[1] Juliano Genari et al. "Quantifying protocols for safe school activities". *PLoS one*. 2022.

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[3] Marcos Sterkel et al. "Tyrosine detoxification is an essential trait in the life history of blood-feeding arthropods". *Current Biology*. 2016.

[4] Marlon A Vergaray Ramirez et al. "On the use of inhibitors of 4-hydroxyphenylpyruvate dioxygenase as a vector-selective insecticide in the control of mosquitoes". *Pest Management Science*. 2022.

Intervention Model

Drug Intervention Framework: The model incorporates a drug-based vector control system targeting mosquito through two intervention strategies. Buildings can be fumigated with the drug at rate $r_{building}$, while humans can receive systemic treatments (inoculation) at rate r_{human}. When mosquitoes encounter treated buildings, they experience drug exposure with probability p_{build}, while mosquitoes biting inoculated humans face exposure probability p_{human}. Each mosquito can only be exposed once per episode, with exposure time t_{drug} recorded upon contact, ensuring realistic single-dose intervention effects.

Mortality Dynamics and Temporal Windows: Drug-induced mortality occurs when mosquitoes are simultaneously within the drug exposure window τ_{drug} and feeding window τ_{feed}. The death probability is proportional to the size of the intersection of both windows as follows:

$$p_{death} = \begin{cases} c_{death} \cdot \frac{t_{fed}+\tau_{feed}-t_{drug}}{min(\tau_{feed},\tau_{drug})}, & if \quad t_{drug} > t_{fed} \\ c_{death} \cdot \frac{t_{drug}+\tau_{drug}-t_{fed}}{min(\tau_{feed},\tau_{drug})}, & if \quad t_{fed} > t_{drug} \end{cases} \tag{1}$$

This intersection captures the temporal overlap between drug presence and metabolic vulnerability during blood digestion.

Intervention Scenarios

Three experimental scenarios were used to evaluate intervention effectiveness:

1. *Baseline* with no intervention control,
2. *Human Inoculation* with $r_{human} = 0.2$, $p_{human} = 0.8$,
3. *Building Fumigation* with $r_{building} = 0.2$, $p_{bldg} = 0.8$.

All scenarios use consistent mortality parameters $c_{death} = 0.6$, $\tau_{drug} = 2.0$ days.

Preliminary Results

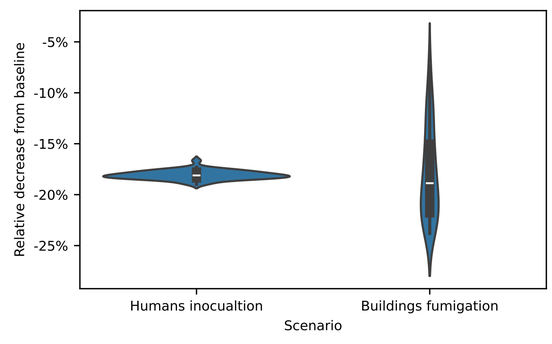

Figure 3. Prevalence decrease from baseline on the two intervention scenarios

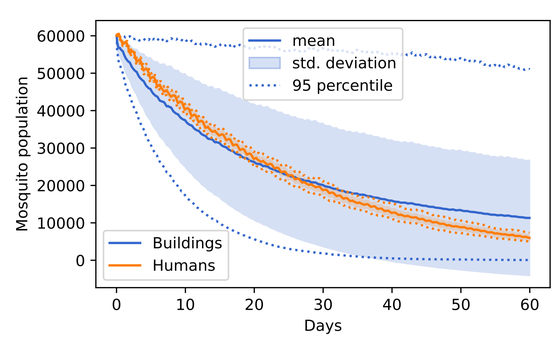

Figure 4. Mosquito population decrease by intervention

These results represent preliminary findings designed to validate whether this modeling approach effectively evaluates drug-based vector control interventions. Figure 3 presents a violin plot showing the relative decrease in infection cases for both interventions compared to baseline, demonstrating that both strategies are effective according to the model. Crucially, while building spraying shows comparable effectiveness to human inoculation, it exhibits substantially greater variability in outcomes. Figure 4 reveals substantial mosquito population suppression under both intervention strategies, with building spraying again displaying broader distributional spread. Human inoculation demonstrates much better controlled variance and is therefore appears to be a more robust intervention strategy, while baseline scenarios (omitted) showed increasing mosquito populations without intervention.

Future Perspectives: These preliminary results establish that this modeling approach can effectively evaluates vector control interventions, providing functional proof-of-concept for the integrated framework. The key finding that interventions appear effective, with human inoculation showing superior robustness due to controlled variance, guides future research directions. Immediate priority involves comprehensive parameter calibration using empirical data from field studies and laboratory experiments to ensure realistic scenario modeling. Subsequent analyses will focus on comparative effectiveness assessment between intervention strategies, with particular emphasis on trade-offs between building spraying's potential effectiveness and human inoculation's superior reliability in diverse epidemiological contexts.

https://docs.comorbuss.org/

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