Eradicating Malaria: Improving a Multiple-Timestep Optimization Model of Malarial Intervention Policy

Taryn Ohashi

Professor Susan Martonosi, Advisor
Professor Chris Towse, Reader

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Abstract

Malaria is a preventable and treatable blood-borne disease whose complications can be fatal. Although many interventions exist in order to reduce the impacts of malaria, the optimal method of distributing these interventions in a geographical area with limited resources must be determined. This thesis refines a model that uses an integer linear program and a compartmental model of epidemiology called an SIR model of ordinary differential equations. The objective of the model is to find an intervention strategy over multiple time steps and multiple geographic regions that minimizes the number of days people spend infected with malaria. In this paper, we refine the resolution of the model and conduct sensitivity analysis on its parameter values.

Contents

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Chapter 1

Malaria, Intervention Techniques, and the Literature

1.1 The Disease

Malaria, a potentially life-threatening disease caused by a blood-borne parasite, infected 216 million people and claimed the lives of an estimated 655,000 people in 2010, most of whom were children in Africa [1]. The parasite (also called a *sporozoite*) causing malaria belongs to the genus Plasmodium and is typically transmitted from person to person through the bites of infected Anopheles mosquitoes [2]. When a mosquito (also called a *vector*) bites an infected human, the mosquito contracts the parasite and can transmit it to the next human it bites. Malaria can also be transmitted through blood transfusions or from an infected mother to her unborn child. An infection becomes fatal when a victim suffers from complications directly

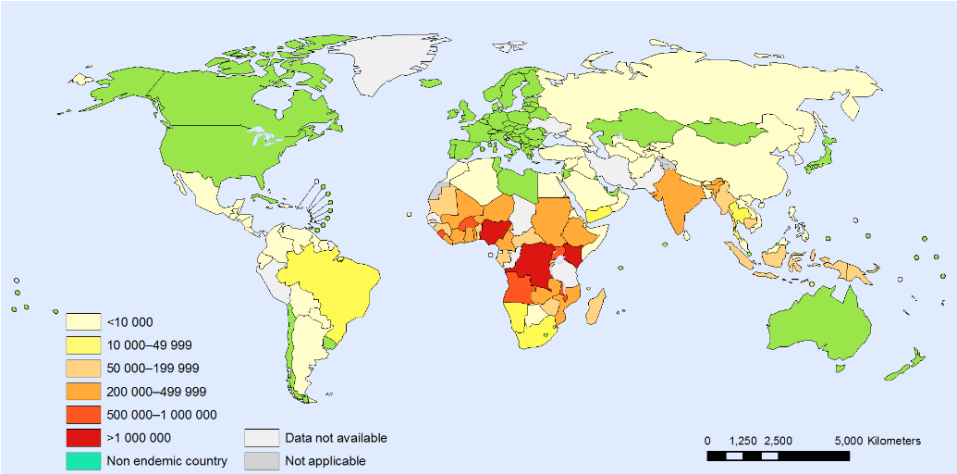

Figure 1.1: Number of reported malaria deaths, 2010 [5].

related to the presence of these sporozoites in his bloodstream. Symptoms include anemia, chills, coma, convulsion, and nausea, while potential complications include brain infection, kidney and liver failure, meningitis, and hemorrhage [2]. Individuals can gain immunity to malaria by continued exposure to malaria parasites, but this natural immunity is lost when exposure ceases [3]. While all non-immune people are at risk, children under five years of age, pregnant women, those with HIV, and the elderly are all more likely to develop these more serious complications [4].

Perhaps what is most frustrating about malaria is that it is both preventable and treatable given the necessary resources. The problem then becomes one of resource scarcity. Developing nations in Africa, where resources are limited, face the most severe consequences of malaria. It is therefore necessary to maximize the impact of the resources that are available. Figure 1.1 shows reported malaria deaths in 2010, by country. We see

that developing areas, particularly countries in Africa, are most affected. Note however, that not all reported malaria deaths are confirmed to be caused specifically by malaria.

In this thesis, we use an operations research framework and a compartmental epidemiology model. The epidemiology model is called an SIR model because it represents the three disease stages: susceptible, infected, and recovered. The objective of the model as a whole is to minimize the number of days people in a population are infected with malaria over a five-year time horizon. The model takes into account the constraints of time and budget, making it a time-dynamic model for malaria intervention choice. The user inputs initial population characteristics over multiple geographic regions, disease modeling parameters specific to the location, and a monetary budget per time step in order to receive a schedule of intervention methods that minimizes the number of deaths due to malaria over the time horizon.

1.2 Intervention Strategies

There are a number of known interventions that either prevent malaria transmission or mitigate its effects. Each intervention has a unique cost and purpose, and actions are either used in a household (e.g. insecticides) or used individualy (e.g. medicine). We briefly discuss the most prominent interventions:

1.2.1 Long-Lasting Insecticidal Net (LLIN)

The first intervention to be used in a physical space is the long-lasting insecticidal net (LLIN). LLINs are used in sleeping quarters to decrease bite rates and the number of mosquitoes in an enclosed area. These nets create a physical barrier between those under it and potential mosquito vectors, and are sprayed with insecticides for additional protection. The treatments remain effective for at least 3 years, even with repeated washings [6]. In the past, LLINs were primarily used by pregnant women and children under 5, but more recently, groups like the World Health Organization have urged all people to use LLINs in malarious areas [6].

1.2.2 Indoor Residual Spray (IRS)

An alternative to LLINs are indoor residual sprays (IRSs), which also decrease the number of mosquitoes in an enclosed area. While there is some controversy on the environmental ramifications of using the spray, the effectiveness of IRS in homes is undeniable [7]. An IRS is sprayed onto walls and other household surfaces with a residual insecticide. Mosquitoes that come in direct contact with these surfaces die, an effect that lasts several months with a single spraying [8].

1.2.3 Intermittent Preventative Treatment (IPT)

Some interventions directly interact with the human body. For example, intermittent preventative treatments (IPTs) help slow the spread of malaria and are used primarily by at-risk populations: infants, school-aged chil-

dren, and pregnant women [9]. IPT is made of sulfadoxine-pyrimethamine and can be taken orally [10]. IPT does not prevent mosquito bites themselves, but rather decreases the risk of contracting malaria from an infectious bite. It is meant to be used regardless if the individual is thought to be infected or not. As its name suggests, it is a preventative action.

1.2.4 Artemisinin-Combination Therapy (ACT)

In the event that malaria has already been contracted, artemisinin-combination therapy (ACT) can be used to treat the disease and prevent complications, increasing the human recovery rate. ACT acts quickly and has a high efficacy rate when used correctly (treatment is typically defined as two doses daily for three days) [11]. In order to prevent misdiagnoses, ACT is usually taken contingent upon a positive rapid diagnostic test (RDT), which detects dangerous parasitic levels in the blood before complications arise.

1.2.5 Vaccine (VAC)

Although not currently available to the public, a vaccination (VAC) for malaria is currently in Phase III of its development [12]. A malaria vaccine would increase human immunity and decrease the overall number of infections. The Malaria Vaccine Technology Roadmap's first goal is to make available a vaccine with a 50% efficacy rate against severe malaria by 2015 [13]. The project's long term goal is to develop a vaccine with a 4 year long, 80% efficacy rate by 2025 [13]. As of late 2012, the vaccine has an efficacy rate of 50% for the first 3-4 months, but its effects seem to wear off within

6 months [14]. As of now, the vaccine's low efficacy rate prevents it from being used clinically.

1.3 Literature Review

The malaria problem has received considerable attention from the academic community, prompting research in various fields to model its treatment, effects, and behavior. We split the literature into two main categories: modeling strategies to combat malaria and modeling the spread of the disease.

1.3.1 Models for Combating Malaria

The first section of the literature focuses on the different ways to lessen the destructive effects of malaria. As previously mentioned, malaria is a preventable and treatable disease, and many intervention strategies exist and are effective. Some analyses therefore identify the most cost-effective interventions, while others are more directly applicable to our project of optimization: which action is most appropriate to take in which setting?

In general, cost-benefit and cost-effectiveness models are used to determine whether or not a certain decision will have a net benefit and, if so, how large this benefit is. It is often up for debate which malaria intervention is the "best" intervention. A systematic review of scholarly work on cost-effective malaria interventions by White et al. concludes that the literature is fairly inconsistent [15]. White et al. survey all English-language, malaria intervention cost-effectiveness studies published between 2000 and 2010 on the electronic online database, PubMed. They identify 55 relevant studies

that examine LLINs, IRS, IPT, vaccines, and malaria diagnostics, and convert all findings into 2009 USD for comparison [15]. IPT for infants and pregnant women are consistently found to be the most cost-effective preventative intervention, but this particular intervention strategy concerns only a fraction of the population. The research also consistently shows that ACT is a highly effective anti-malarial drug. These findings are consistent with the actions most consistently chosen by this thesis's model: ACT and IPT. However, researchers differ in opinion on whether LLIN or IRS is more cost-effective [15]. In general, papers like those surveyed by White et al. help to identify which specific intervention method to pursue from an economic standpoint.

Other papers evaluate the effectiveness of a specific intervention across multiple suppliers. In the specific context of identifying the most beneficial RDT, Lubell et al. develop an online, interactive model, the RDT Decision Support Model, based on a decision-tree and cost-benefit framework to compare different types of RDTs given a particular setting [16]. They assign monetary values to "consequences of diagnosis and treatment" and allow the program's user to input their own parameters, "making the model adaptable to different antimalarial and RDT costs" [16]. Models like this one are useful when there are several suppliers of an intervention type, or when some brands of an intervention are more effective than others for specific populations.

Some research models tackle the problem of logistics. Supply chain management is especially important in the context of malaria because several distribution services are often needed to transport goods and services

to remote, developing towns and villages. Min considers distribution dynamics, logistics infrastructure, supply chain variables, and customer needs to propose an integrated supply chain mapping model (SCMM) for anti-malarial drugs (e.g. ACT, IPT) [17]. He identifies four major anti-malarial drug supply chain strategies. Min suggests that pharmaceutical manufacturers use existing distribution channels in sub-Saharan Africa, create local drug storage facilities throughout the area to aid the timeliness of treatment, overcome local trade and regulatory barriers that prevent a free market, and outsource drug distribution services [17]. While these suggestions may demand resources such as time and money, Min asserts that these efforts would enhance the accessibility of anti-malarial drugs.

Other models examine spatial effects. Larson et al. use a regression model to investigate the relationship between LLIN possession/use and a household's distance from health services [18]. They find an inverse relationship between the two: as the distance between a household and a health facility increases, the possession of LLINs decreases. These results are statistically significant and hold when controlling for age, gender, the ratio of nets to children in a household, community net possession and use, and household wealth [18]. Others use results from this paper and those like it to identify the optimal locations in which to move or build health services hubs.

Spatial models are not limited to distribution logistics: Cummins et al. model mosquitoes' host-seeking behavior, predicting malaria's transmission dynamics [19]. The model is used to describe the effect of spatial heterogeneity on the contact rate between mosquitoes and humans [19].

They find that mosquito-human contact is highest when there is sufficient time for mosquitoes to find human hosts or leave the specified area entirely. They also find that the per-capita number of contacts is smaller in a large group of humans than in a small group, controlling for the size of the space. These results are intuitive and are consistent with similar literature.

A software program created by Smith et al., *openmalaria*, offers a multi-faceted look at the malaria problem by letting the user input his own data to explore the effects of intervention methods on infection, morbidity and mortality, health services usage, and cost [20]. While the research mentions the use of stochastic methods to predict such impacts, there is no documentation of how the simulation explicitly operates, so it is difficult to extend this work. *Openmalaria* does not take budget into consideration for their optimal solutions and considers malaria transmission dynamics for only a single isolated population.

The most influential model for this specific project is that of Dimitrov et al. [21]. The authors combine several types of models in order to produce a single large-scale, geographic optimization model [21]. More specifically, they use a Markov Decision Process (MDP) to choose optimal intervention actions given resource constraints over a spatial framework. By dividing a region into several small cells in a grid-like fashion, Dimitrov et al. use a linear program to identify the actions to be used in each cell given intervention plans, a budget, and locations of supply distribution centers.

This thesis extends Dimitrov et al.'s model to consider interventions taken annually over a fixed number of years in a non-spatial context. The model, initially developed by Hoeger et al., accounts for the differential im-

pacts each intervention type has on the spread of malaria in the population and is refined in this thesis [22].

1.3.2 Models of the Spread of Malaria

This second portion of the literature comes from the field of epidemiology. Epidemiologists are concerned with causes, effects, and patterns of health-related ideas. Their work includes the modeling of disease spread, which is useful to the model refined in this thesis. Researchers model the spread of infectious diseases by compartmentalizing human populations and using differential equations. Common compartments include those susceptible (S), infected (I), and recovered (R). SIR models are often generic to many classes of infectious diseases, but many scholars offer improvements that better represent the spread and transmission of malaria.

Mandal et al. survey the most influential SIR-based models specific to malaria [23]. These models stem from the Ross Model of the early 1900s [24]. The Ross Model analyzes the relationship between the number of mosquitoes in an area and the number of malaria cases in humans by using a two-equation system of differential equations, assuming a constant human population. This model is described as "the simplest possible theoretical description consistent with the data [that was] available" at the time, but epidemiologists have since made improvements [23]. Newer, more complex, models now take into account factors such as latency and incubation periods, at-risk groups, and acquired immunity.

In more recent years, researchers have expanded models to capture immunity loss effects. These models, like Koella and Antia's, account for the

fact that natural malarial immunity fades without consistent exposure [25]. The model uses a system of three differential equations (representing S, I, and R), but differs from the Ross model in its attention to immunity behavior. They include calculated immunity loss and inoculation rates, which are functions of parameters such as the birth rate, number of mosquitoes, incubation period, amongst others, in their SIR model. The Koella and Antia model therefore enhances the Ross Model, but still assumes a constant population.

Some models, such as Anderson and May's, call for even more specific parameters in hopes of creating a more accurate model of the dynamics of malaria [26]. In their work, the traditional SIR model becomes a Susceptible, Exposed, Infected, Susceptible ($SEIS$) model that exploits the latency period of both infected mosquitoes and humans. The authors consider mosquitoes and human hosts separately such that the mosquitoes are divided into compartments S_m, E_m, and I_m, distinct from the human compartments S_h, E_h, and I_h. Their system of four differential equations models the time evolution of the exposed and infected classes for both mosquitoes and humans [26]. The four equations model the entire system since the remaining two compartments, S_m and S_h, can be calculated given the values of the E and I compartments. The inclusion of the latency periods reduces long term prevalence of both I_h and I_m, providing a more complex interpretation of malaria's effect on a human population than those models which did not include a latency period [23].

Other models utilize the E class and the separation of mosquitoes and humans to create categories that specific epidemiological models can fall

into: SIS, SIR, $SIRS$, SEI, $SEIS$, and $SEIRS$. A particularly influential piece by Chitnis et al. uses an $SEIR$ framework that allows for changing population levels [27]. The systems of equations model the spread of malaria within humans and mosquitoes separately, and create N classes that account for human and mosquito population sizes as they vary with time. This paper also introduces a reproductive number, R_0, that represents the number of secondary cases that one infected individual will cause through the duration of the infectious period [27]. Chitnis et al. then conduct bifurcation analysis to find that a disease-free equilibrium is locally stable when $R_0 < 1$ and locally unstable when $R_0 > 1$.

While some models in the literature are non-specific to malaria and can therefore be applied to better-understood diseases, it is critical to choose an epidemiological model that has extant, sufficient data for parameters when dealing with malaria. Since malaria is primarily a problem in developing nations where data collection is rare, it can be difficult to apply complex models because they rely on data that simply do not exist in much of the developing world. The data problem is the primary reason for this thesis's reliance on the relatively simple, Koella and Antia SIR model. In order to make the thesis's SIR model more realistic, methods used in Chitnis et al. regarding the N class and varying population size can be incorporated into the framework of the differential equations, as discussed in Chapter 6.

The remainder of the thesis proceeds as follows: Chapter 2 introduces the integer linear program framework of the optimization model, Chapter 3 presents the specific SIR model whose data is used as input to the linear program, Chapter 4 discusses a problem with the preliminary results of the

model, Chapter 5 includes sensitivity analysis of the model, and Chapter 6 suggests further work to be done on this project.

Chapter 2

Integer Linear Program

The model in this thesis has two main components: an integer linear program (ILP) and a compartmental epidemiological SIR model of differential equations. This two-part model finds an optimal sequence of intervention strategies to use over a five year time horizon in a given area. The goal of the program is to minimize the number of days people in a population spend infected with malaria. The SIR model is needed to create disease transmission data necessary to the solution of the ILP. This section describes the purpose and functionality of the ILP in particular.

2.1 Model Formulation

While it would be ideal to use a combination of intervention strategies on every person in a population to combat malaria, resources such as time and money are limited. It is therefore crucial to make best use of the resources that are available. In this case, the goal is to minimize the number of days

people are infected with malaria given a monetary budget and a five year time horizon. The ILP optimizes this outcome, considering inputted budget constraints and intervention effectiveness.

Given a set of cities and geographic regions, across which the population and disease transmission dynamics might differ, and a set of possible interventions, each having its own cost and each affecting disease transmission differently, the model selects which intervention or combination of interventions to apply in each region on an annual basis in order to minimize total illness over a longer time horizon. The set of chosen interventions is restricted by an annual budget. An ILP is used to solve this problem, taking as input malaria population state dynamics from an SIR model.

2.1.1 The Integer Linear Program

The indices of the decision variables and parameters used explicitly in the model can be described as follows. p represents the population state. A population state is defined by the percentages of a city's population that are susceptible, infected, and recovered. A city is in a particular population state when its population can be defined by the population state's percentage breakdown. g represents the geographic region that a city falls in. There are two regions included in my analysis: rural and urban, whose population levels, costs, and losses differ from each other. t represents the year and i represents the action performed.

Decision variables:

$P_{pgt} =$ number of cities in population state p in geographic region g at time t.

a_{ipgt} = number of cities in population state p for which action i is performed at time t in geographic region g.

Parameters:

b_t = budget at time t

I_{pg} = initial number of cities in population state p in geographic region g

L_{ipgt} = number of person days of malaria infection during year t when performing action i in population state p in geographic region g at time t

c_{ig} = cost for performing action i in geographic region g

OUT_{pg} = set of interventions that when applied to a city in population state p in geographic region g will cause the state to evolve out of state p

IN_{pg} = set of $(\hat{i}, \hat{p}, \hat{g})$ combinations that will evolve into state p in geographic region g

$$\min_{a} \quad \sum_{t,i,p,g} L_{ipgt} a_{ipgt} \tag{2.1}$$

$$\text{s.t.} \quad \sum_{i,p,g} c_{ig} a_{ipgt} \leq b_t \qquad \forall t \tag{2.2}$$

$$\sum_{i} a_{ipgt} = P_{pgt} \qquad \forall p, g, t \tag{2.3}$$

$$P_{p,g,1} = I_{pg} \qquad \forall p, g \tag{2.4}$$

$$P_{p,g,t+1} = P_{pgt} - \sum_{\hat{i} \in \text{OUT}_{pg}} a_{\hat{i}pgt} + \sum_{(\hat{i},\hat{p},\hat{g}) \in \text{IN}_{pg}} a_{\hat{i}\hat{p}\hat{g}t} \qquad \forall p, g, t \tag{2.5}$$

$$a_{ipgt}, P_{pgt} \geq 0, \quad \text{integer} \qquad \forall i, p, g, t \tag{2.6}$$

2.1.2 Interpreting the ILP

Consider the model's objective function and constraints individually:

- The objective function (2.1) minimizes the total loss accumulated as a result of the actions taken.
- The first constraint (2.2) is the budget constraint. The ILP cannot choose more actions than the budget can afford in each time period. The user inputs a budget for every time step that must be shared across all regions and cities.
- Constraint (2.3) requires that the ILP choose an action for every city in each time step. Given a budget, many cities may be forced to "do nothing" in a given year if the budget cannot accommodate actions to be taken in all cities in all time steps.
- Constraint (2.4) defines the initial population I_{pg} to be equal to the city distribution at time $t = 1$, or $P_{p,g,t=1}$.
- Constraint (2.5) is a flow-balance constraint. It mandates that at any given time step $t+1$, the number of cities in a specific population state p in geographic region g be equal to the number of cities that remain in this population state from the past year less the number of cities whose actions take them out of the population state plus the number of cities whose actions bring them into the population state.
- Constraint (2.6) makes this linear program an integer linear program. It states that the decision variables, a_{ipgt} and P_{pgt}, must be nonnega-

tive integers. The ILP cannot interpret fractions of cities.

2.2 Input Data

The parameters b_t, I_{pg}, and c_{ig} are chosen directly by the model's user to be input into the ILP. Losses (L_{ipgt}, the number of person days of malaria infection during year t when performing action i in population state p in geographic region g at time t) on the other hand, are determined from the output of the SIR model, as discussed in Chapter 3.

2.3 Population Dynamics

The population states p are defined by the percentages of the population that fall into each of the following categories: susceptible, infected, and recovered/immune. These categories are referred to as compartments and hence, the SIR model is called a compartmental model. A susceptible human is one who is not infected with malaria, but has the potential to be in the future. An infected person has contracted malaria and thus carries the malaria-inducing parasite. Lastly, recovered/immune beings have survived a previous malaria incidence. Often times, a recovered person still carries trace amounts of the malaria parasite in their bloodstream such that they become temporarily immune to the disease. The movement from S to I to R and back to S represents the typical progression of someone who contracts malaria and survives.

Each compartment, susceptible, infected, and recovered/immune, con-

tains the percentage of the population that falls within that category. Then the sum of the three compartments must equal 1. For example, in a city that can be described by the population state of $\begin{bmatrix} 0.50 & 0.40 & 0.10 \end{bmatrix}^T$, 50% of the people are susceptible, 40% are infected, and 10% are recovered. Population states are therefore discretized according to a user-specified resolution; for example, one percentage point.

The ILP's choice of action in a given city and year affects the disease dynamics and changes the population state of the city in the subsequent year. Given a city's initial population state p and choice of action i, the SIR model determines the city's new population state $p'(p, i)$ at the start of the next year. This transition from population state p to population state p' under action i is stored in a lookup table that serves as input to the ILP. The SIR model also calculates the loss function representing the number of person days of malaria infection during year t given action i, population state p, and geographic region g.

The specific way in which the SIR model determines interventionary actions' and time's effects on the way a population is compartmentalized is described ahead.

Chapter 3

SIR Model

The SIR model in this thesis is used to describe the evolution of a population's distribution into the three compartments, susceptible, infected, and recovered/immune, over time. Some population states are inherently more desirable than others–it would be better for a population to be described by the vector $\begin{bmatrix} 0.80 & 0.10 & 0.10 \end{bmatrix}^T$ than $\begin{bmatrix} 0 & 0.90 & 0.10 \end{bmatrix}^T$ because a society would rather have 10% of its population infected with malaria than 90%. It is therefore crucial to the solution of the ILP to know how the use of intervention methods affects a city's population state evolution over time.

3.1 Model Formulation

This SIR model, as adapted from Koella and Antia, assumes a constant population over time [25]. This model, a system of three differential equa-

tions, is the model used in Hoeger et al [22]. It is defined as follows:

$$\begin{aligned}\frac{dS}{dt} &= \phi - (\phi + h + v)S + \rho R \\ \frac{dI}{dt} &= hS - (r + \phi)I \\ \frac{dR}{dt} &= rI - (\rho + \phi)R + vS,\end{aligned}$$

where $S =$ proportion of population that is susceptible,
$I =$ proportion of population that is infected,
$R =$ proportion of population that is recovered/immune,
$\phi =$ birth/death rate (set equal to each other so population size is constant),
$h =$ inoculation rate,
$\rho =$ rate of immunity loss,
$v =$ vaccine efficacy rate (if no vaccine is available, then $v = 0$), and
$r =$ recovery rate of infected people.

The inoculation rate h and rate of immunity loss ρ are functions of I. They are calculated as follows [25]:

$$\begin{aligned}h &= mbd^2 e^{-\mu\tau}\frac{I}{\mu + dbI} \\ \rho &= \frac{(h+\delta)e^{-(h+\delta)\omega}}{1 - e^{-(h+\delta)\omega}},\end{aligned}$$

where $m =$ mosquitoes per human,
$b =$ proportion of bites that lead to infection,
$d =$ bites per time,
$\mu =$ mosquito mortality rate,
$\tau =$ mosquito incubation rate, and
$\omega =$ duration of immunity.

3.2 Parameter Values

Table 3.1 displays the parameter values used in the case where the action is to do nothing. These are also referred to as baseline parameters and are gathered from the literature. They are representative of populations where malaria is endemic and are reported as daily rates [23], [28], [29].

Parameter	**Baseline Value**
ϕ, birth rate [1]	1.054×10^{-4} days^{-1}
r, recovery rate	$1/180$ days^{-1}
ω, duration of immunity	274 days
d, bites per time	0.25 days^{-1}
b, proportion of bites that lead to infection	0.35 days^{-1}
m, mosquitoes per human	20
μ, mosquito mortality rate	0.275 days^{-1}
τ, mosquito incubation period	10 days
v, vaccine efficacy	0

Table 3.1: Baseline parameter values for the SIR model [23], [28], [29].

[1] It is essential to note that birth and death rates are reported annually and given as births or deaths per 1,000 people. To convert the statistic to an annual percentage, divide the number of births or deaths by 1,000 and multiply by 100%. To convert to the daily rate

This SIR model is convenient because the parameter values have already been estimated in the literature. More complex models require parameters that are not collected in developing areas where malaria is most prevalent.

Intervention actions' specific effects on the parameters used in the SIR model are summarized in Table 3.2. Hoeger et al. used information from several sources to estimate the effect each intervention would have on the parameters [22] [30] [31] [32] [33] [34] [35]. These new parameter values replace the baseline parameter value affected depending on which action is chosen by the ILP. For example, since LLINs are used as a physical barrier between human hosts and vectors, they decrease the bites per time d when used. Then the baseline value of $d = 0.25$ is replaced by the lower value $d = 0.163$ whenever the ILP chooses to use LLINs. Similarly, ACT is utilized as a medicine to help already infected individuals heal. Therefore the recovery rate r increases when ACT is used. IPT is a preventative treatment that decreases the proportion of bites that lead to infection b, and IRS kills mosquitoes who come in contact with sprayed areas, thus decreasing the number of mosquitoes per human m. Vaccine efficacy rates increase when actually used, so vaccine efficacy v increases when included in the model.

The monetary costs of implementing each intervention are held con-

given in the table, calculate:

$$(1+\delta)^{365} = 1 + (\text{yearly rate})$$

$$\delta = \sqrt[365]{1 + (\text{yearly rate})} - 1$$

Action Taken	Effect on Parameter	New Parameter Value
None	None	–
LLIN	$\downarrow d$	0.163
ACT	$\uparrow r$	0.05
IPT	$\downarrow b$	0.245
IRS	$\downarrow m$	8.56
VAC	$\uparrow v$	0.00129

Table 3.2: This table charts the parameter values that replace the baseline parameter values if a particular action is chosen. Notation: $\downarrow d$ indicates that an LLIN decreases parameter d, bites per time [30] [31] [32] [33] [34] [35].

stant and are described in Table 3.3 [36].

Intervention Method	Cost (USD/person)
Intermittent Preventative Treatments (IPT)	0.18
Artemisinin-based Combination Therapy (ACT)	0.67
Rapid Diagnostic Test (RDT)	0.70
Indoor Residual Spraying (IRS)	1.08
Long Lasting Insecticide-treated Nets (LLIN)	1.17

Table 3.3: Cost per action per person [36].

3.3 *SIR* Model and the ILP

The information generated by the SIR model is necessary for the ILP to find an optimal solution of intervention strategies. Not only does the SIR model dictate how actions affect disease transmission and population state dynamics, but it calculates the losses L_{ipgt} incurred by taking action i in population state p in geographic region g at time t.

The losses L_{ipgt} are calculated using a mid-point Riemann sum under the infected population curve as produced by the I differential equation in

the SIR model. This loss explicitly represents the product of the number of people who are infected with malaria and the number of days these people spend infected. The objective of the ILP is then to minimize the losses incurred by actions across the time period, all actions, all population states, and all geographic regions.

Chapter 4

Rounding Errors and Resolution Improvement

Because Hoeger et al. discretized population states before using them as inputs to the ILP, there was a good possibility that rounding errors could distort the choice of intervention allocations [22]. In particular, it was possible that the model was consistently rounding the I compartment down to 0%, telling the ILP to choose the "none" action. This rounding toward 0 would also artificially decrease the real loss of the system. Therefore, in this thesis, we halve the resolution of the population state vectors from increments of two percentage points (as used in Hoeger et al.) to increments of one percentage point.

Ordinarily, one would round each population state value to the nearest resolution increment. However, because the population percentages in each SIR compartment must sum to 1, one of the three compartments will

need to be rounded to the *farther* resolution increment. We use the same technique as Hoeger et al. in the rounding process. We select the compartment with the largest percentage of the population to round to the farther increment; this reduces percent rounding error. For example, assume that the resolution is set to 0.1 and that the population state needing to be rounded is $\begin{bmatrix} 0.33 & 0.53 & 0.14 \end{bmatrix}^T$. The infected class, accounting for 53% of the population, is the largest class, so it is rounded to 0.6 rather than to 0.5 as we might expect. The susceptible and recovered classes are rounded to their nearest increments of 0.3 and 0.1, respectively, as expected. Using this algorithm, the population state $\begin{bmatrix} 0.33 & 0.53 & 0.14 \end{bmatrix}^T$ is rounded to $\begin{bmatrix} 0.3 & 0.6 & 0.1 \end{bmatrix}^T$, which still sums to 1.

4.1 Action Effectiveness Sensitivity

Since the exact effects intervention methods have on the transmission dynamics of malaria are uncertain, Hoeger et al. explore a range of action effectiveness [22]. We continue this analysis in order to thoroughly compare the resolution's effect on ILP output.

While it makes intuitive sense which parameters in the SIR model are affected by each intervention, finding specific statistics on the magnitude of their effects is difficult. The effects of actions are usually reported in ranges. In order to capture this trend, $\pm 15\%$ and $\pm 30\%$ intervals are created for each parameter affected by an action to simulate five scenarios: optimistic, slightly optimistic, neutral, slightly pessimistic, and pessimistic, where the "neutral" scenario represents the average parameter value given an action

(the neutral values are also expressed in Table 3.2).

The optimistic scenario will be referred to as scenario 1, slightly optimistic as scenario 2, neutral as scenario 3, slightly pessimistic as scenario 4, and pessimistic as scenario 5. The parameter values that replace the baseline values given in Table 3.1, dependent on scenario, are reported in Table 4.1 and are identical to the values used in Hoeger et al. [22].

Action Taken	**Effect on Parameter**	**Scenario 1**	**Scenario 2**	**Scenario 3**	**Scenario 4**	**Scenario 5**
None	None	–	–	–	–	–
LLIN	$\downarrow d$	0.114	0.139	0.163	0.187	0.212
ACT	$\uparrow r$	0.065	0.058	0.05	0.043	0.035
IPT	$\downarrow b$	0.172	0.208	0.245	0.282	0.319
IRS	$\downarrow m$	5.99	7.28	8.56	9.84	11.13
VAC	$\uparrow v*$	0.00158	0.00144	0.00129	0.00113	0.00096

Table 4.1: This table charts the parameter values that replace the baseline parameter values if a particular action is chosen in the pessimistic, slightly pessimistic, neutral, slightly optimistic, and optimistic scenarios. Notation: $\downarrow d$ indicates that an LLIN decreases parameter d, bites per time.

4.2 Resolution Change's Effects on Intervention Sequences

We halve the resolution from 0.02 to 0.01 in order to analyze how rounding errors and resolutions affect the output schedule of interventions. This alteration requires the creation of a new data set with new calculated losses. We hold all else constant with Hoeger et al.'s analysis for the purposes of comparison: the initial population distribution, action costs, and budget are the same as those used in their work [22].

For the purposes of analysis, the following initial conditions are set. We allot 10 cities into the urban region and 10 cities into the rural region for a total of 20 cities. Each of these 20 cities begin at the population state $\begin{bmatrix} 0.50 & 0.18 & 0.32 \end{bmatrix}^T$ and have populations of 1,000 in rural cities and 10,000 in urban cities. Interventions for the entire system of 20 cities must stay within a budget of \$35,000/year. The costs for each action are described in Table 3.3.

Table 4.2 records the minimized objective values (total loss, or number or days people in a population spend infected with malaria) for each scenario run with resolutions of 0.02 and 0.01 given the aforementioned initial conditions. It also displays the percentage difference in the objective value, the number of days people in a population spend infected with malaria, relative to the 0.02 resolution case.

Scenario	**Res=0.01 OV**	**Res=0.02 OV**	**Percentage Difference**
1	6,849.09	6,848.08	+0.01%
2	17,740.55	11,928.00	+48.72%
3	18,441.76	17,284.26	+8.70%
4	23,960.20	24,346.15	-1.59%
5	23,656.85	23,684.11	-0.11%

Table 4.2: Objective values (OV) for the 0.01 and 0.02 resolution cases, and the percentage difference relative to the 0.02 resolution OV.

Holding all else constant, the objective values differ across resolutions. This means that resolution and the rounding algorithm do indeed affect ILP output. The difference in objective value in scenario 2 is particularly significant, suggesting that there may also be a difference in the intervention schedule amongst the resolutions. Since the percentage differences in

objective value differ across scenarios, it is clear that the effect of resolution on objective value is nonlinear.

Tables 4.3 and 4.4 show, for each scenario and geographic region, the optimal intervention sequences cities should take over a five-year time horizon as given by the ILP's output. The intervention sequence "none, none, ACT, none, none" means a city should do nothing when $t = 1, 2, 4, 5$ and use ACT when $t = 3$. The tables also show which population state (denoted here as (S, I) and R can be calculated as $1 - S - I$) a city will end up in at $t = 6$ if it follows an intervention sequence in the stated scenario and region. Since many cities are to follow the same intervention sequence, the number of cities that the scenario, region, sequence, and final population state applies to is also included. The initial condition of 10 rural cities and 10 urban cities is preserved throughout, and thus the sum of the number of cities in each scenario and region equals 10.

The intervention sequences in Table 4.3 are from the 0.01 resolution case, and Table 4.4 shows sequences for the 0.02 resolution case. A difference in these two tables indicates that a change in resolution has an effect on the chosen interventions.

As evident from these tables, a change in resolution does indeed produce different intervention strategies, which, in turn, yields differences in objective values, intervention sequences, and final population distributions. While the differences in these three metrics are generally subtle, we observe that the larger the difference in objective value (see Table 4.2), the greater the difference in action paths and final population distributions. This is to be expected: differences in action effectiveness allow for different

losses, which are used as input into the ILP. In both resolution cases however, ACT and IPT are the two most commonly used intervention methods, which is consistent with the cost-effectiveness literature (discussed in Section 1.3.1).

In scenario 1, the most optimistic of the scenarios where intervention actions are most effective, the objective values differ by just 0.01% when the resolution is halved from 0.02 to 0.01. The intervention action paths are for the most part very similar in each case. Only 2 of the 5 action paths differ at all and even still, the differences are small: the same intervention strategies are used, but in different orders. Cities end up in similar, but not identical final destination cells.

The largest discrepancies between the two resolution cases occurs in scenario 2, where the percentage difference in objective value is 48.72%. The differences are most prominent in the rural case where the order of interventions to be given are varied within otherwise similar action paths. The other most obvious distinction between the two cases is that while three action paths in the 0.02 case rely on vaccinations for the final action, vaccines are not used at all in the 0.01 case. Because the 0.02 case vaccinates at $t = 5$, the recovered/immune population share is significantly higher at the final population state in the 0.02 case than in the 0.01 case.

Scenario 3, the neutral or "average" scenario, also experiences a large difference in objective value when the resolution is halved. Unlike scenario 2, both the rural and urban settings experience discrepancies. The urban scenarios even differ in their numbers of unique action paths. This is the only time throughout this testing that this type of difference occurs. While

we are able to directly compare specific action paths between resolutions in all other scenarios, this particular urban case defies the norm with 4 distinct intervention sequences in the 0.01 case and 5 in the 0.02 case. Furthermore, cities experience nonzero infected and high levels of recovered populations for the first time in the 0.01 case. This likely contributes to the lower resolution's higher objective value. Lastly, the specific intervention methods of IPT and ACT are often interchanged between resolution cases. For example, the action path IPT, IPT, IPT, IPT, IPT in the 0.01 case corresponds to the action path IPT, IPT, IPT, IPT, ACT in the 0.02 case. This suggests that, in the 0.01 case, more resources are put toward the prevention of malaria rather than curing those who have already contracted the disease.

The number and magnitude of discrepancies fall in the more pessimistic scenarios. In scenarios 4 and 5, the action paths themselves are identical across resolutions, but the final population distributions differ.

Overall, the extreme scenarios (most optimistic and pessimistic) see the smallest variations in objective value, optimal action path, and final destination population distributions. Intuitively, this is not surprising: when actions are very effective as they are in the optimistic scenario, a population enjoys a smaller loss when intervention strategies are pursued no matter what. In optimistic scenario 1, actions affect the population distribution in a significant manner. Therefore, the few actions that are chosen are very effective, independent of the population state and region in which they are used in. So, changing how the program rounds population states has little effect on the actions chosen. On the other hand, when actions are relatively ineffective as they are in scenarios 4 and 5, interventions do

not sway the natural progression of the population as dictated by the SIR model quite as well. In these extreme cases, the lack of power of the intervention methods outweighs the rounding inconsistencies presented by changes in resolution, resulting in similar action paths and objective values in the 0.01 and 0.02 cases.

Scenario	No. Of Cities	Intervention Sequence	Final Population State
1, rural	6	none, none, ACT, none, none	$(0.98, 0)$
1, rural	2	none, ACT, none, none, none	$(0.99, 0)$
1, rural	2	ACT, none, none, VAC, none	$(0.93, 0)$
1, urban	5	ACT, none, none, none, none	$(1, 0)$
1, urban	5	none, ACT, none, none, none	$(0.99, 0)$
2, rural	7	IPT, IPT, IPT, IPT, ACT	$(0.72, 0)$
2, rural	1	ACT, IPT, IPT ,ACT, IPT	$(0.93, 0)$
2, rural	1	IPT, ACT, IPT, IPT, IPT	$(0.99, 0)$
2, rural	1	IPT, IPT, ACT, IPT, IPT	$(0.98, 0)$
2, urban	3	ACT, IPT, IPT, ACT, IPT	$(0.93, 0)$
2, urban	3	IPT, ACT, IPT, IPT, IPT	$(0.99, 0)$
2, urban	3	IPT, IPT, ACT, IPT, IPT	$(0.98, 0)$
2, urban	1	IPT, IPT, IPT, IPT, ACT	$(0.72, 0)$
3, rural	7	IPT, IPT, IPT, IPT, IPT	$(0.08, 0.13)$
3, rural	1	IPT, IPT, IPT, ACT, ACT	$(0.50, 0.01)$
3, rural	1	IPT, ACT, IPT, IPT, IPT	$(0.99, 0)$
3, rural	1	ACT, IPT, ACT, IPT, IPT	$(0.98, 0)$
3, urban	3	ACT, IPT, ACT, IPT, IPT	$(0.98, 0)$
3, urban	3	IPT, ACT, IPT, IPT, IPT	$(0.99, 0)$
3, urban	3	IPT, IPT, IPT, ACT, ACT	$(0.50, 0.01)$
3, urban	1	IPT, IPT, IPT, IPT, IPT	$(0.08, 0.13)$
4, rural	9	IPT, IPT, IPT, IPT, IPT	$(0.07, 0.12)$
4, rural	1	ACT, ACT, ACT, ACT, ACT	$(0.43, 0.03)$
4, urban	7	IPT, IPT, IPT, IPT, IPT	$(0.07, 0.12)$
4, urban	3	ACT, ACT, ACT, ACT, ACT	$(0.43, 0.03)$
5, rural	9	IPT, IPT, IPT, IPT, IPT	$(0.06, 0.11)$
5, rural	1	ACT, ACT, ACT, ACT, ACT	$(0.35, 0.04)$
5, urban	7	IPT, IPT, IPT, IPT, IPT	$(0.06, 0.11)$
5, urban	3	ACT, ACT, ACT, ACT, ACT	$(0.35, 0.04)$

Table 4.3: Intervention sequences and final cell destinations given a 0.01 resolution.

Scenario	No. Of Cities	Intervention Sequence	Final Population State
1, rural	6	none, none, ACT, none, none	$(0.98, 0)$
1, rural	2	ACT, none, none, none, none	$(1, 0)$
1, rural	2	none, ACT, VAC, none, none	$(0.98, 0)$
1, urban	5	ACT, none, none, none, none	$(1, 0)$
1, urban	5	none, ACT, none, none, none	$(1, 0)$
2, rural	7	IPT, IPT, IPT, ACT, IPT	$(0.92, 0)$
2, rural	1	ACT, IPT, IPT, IPT, VAC	$(0.76, 0)$
2, rural	1	IPT, ACT, IPT, IPT, VAC	$(0.76, 0)$
2, rural	1	IPT, IPT, ACT, IPT, VAC	$(0.76, 0)$
2, urban	3	ACT, IPT, IPT, IPT, IPT	$(1, 0)$
2, urban	3	IPT, ACT, IPT, IPT, IPT	$(1, 0)$
2, urban	3	IPT, IPT, ACT, IPT, IPT	$(0.98, 0)$
2, urban	1	IPT, IPT, IPT, ACT, IPT	$(0.92, 0)$
3, rural	7	IPT, IPT, IPT, IPT, ACT	$(0.70, 0)$
3, rural	1	ACT, IPT, IPT, ACT, IPT	$(0.92, 0)$
3, rural	1	IPT, ACT, IPT, IPT, IPT	$(1, 0)$
3, rural	1	IPT, IPT, ACT, IPT, IPT	$(0.98, 0)$
3, urban	3	IPT, IPT, ACT, IPT, IPT	$(0.98, 0)$
3, urban	3	IPT, ACT, IPT, IPT, IPT	$(1, 0)$
3, urban	2	ACT, IPT, IPT, ACT, IPT	$(0.92, 0)$
3, urban	1	IPT, IPT, IPT, IPT, ACT	$(0.70, 0)$
3, urban	1	ACT, IPT, IPT, ACT, ACT	$(0.92, 0)$
4, rural	9	IPT, IPT, IPT, IPT, IPT	$(0.08, 0.12)$
4, rural	1	ACT, ACT, ACT, ACT, ACT	$(0.44, 0.04)$
4, urban	7	IPT, IPT, IPT, IPT, IPT	$(0.08, 0.12)$
4, urban	3	ACT, ACT, ACT, ACT, ACT	$(0.44, 0.04)$
5, rural	9	IPT, IPT, IPT, IPT, IPT	$(0.06, 0.12)$
5, rural	1	ACT, ACT, ACT, ACT, ACT	$(0.36, 0.04)$
5, urban	7	IPT, IPT, IPT, IPT, IPT	$(0.06, 0.12)$
5, urban	3	ACT, ACT, ACT, ACT, ACT	$(0.36, 0.04)$

Table 4.4: Intervention sequences and final cell destinations given a 0.02 resolution.

Chapter 5

Parameter Sensitivity Analysis

We conduct parameter sensitivity analysis in order to better understand the effect of parameters on the output of the ILP. This analysis is especially important for this type of humanitarian logistics problem because data is imprecise and scarce. The estimates of the parameter values used in this thesis come from the wide ranges of numbers presented in the literature [23], [28], [29]. Before the methods and outputs of this model and others like it can be used in practice, policy makers should understand how much uncertainty they have in the input of their data.

5.1 Varying Parameter Values

Since malaria transmission parameter values are difficult to obtain in developing areas, a wide range of values have been published for each specification. To both accommodate varying estimates as well as conduct sensitivity analysis, we explore three cases: one optimistic, one pessimistic, and one

control case.

The optimistic case assumes the least threatening parameter values reported in the literature. Specifically, a higher recovery rate r, a higher duration of immunity ω, lower bites per time b, and fewer mosquitoes per human m, relative to the average statistic found in the literature [23], [28], [29].

On the other hand, the pessimistic case assumes the most threatening parameter values reported in the literature. The parameters move in opposite directions than in the optimistic case: the recovery rate r decreases, duration of immunity ω decreases, bites per time b increases, and the number of mosquitoes per human m increases relative to the average statistic.

We create a control case for comparison purposes. We use the same parameters as reported in Table 3.1 and Hoeger et al. These parameters generally represent the average of the given range of values [22].

The specific parameter values assumed in the optimistic, pessimistic, and control cases are listed in Table 5.1. These values are considered the baseline parameters in each case. That is, these are the values the SIR model uses in the case of no action. Interventions further increase or decrease these parameters as described in Table 4.1. It is important to note that human birth rate ϕ, mosquito mortality rate μ, and mosquito incubation period τ are held constant across all three cases. This is because the effects of human/mosquito population and disease behavior on disease progression are not inherently obvious. Similarly, vaccine efficacy v is held constant because, at the time of writing, malaria vaccine efficacy rates have not been confirmed or published.

Parameter	Optimistic Value	Control Value	Pessimistic Value
ϕ, birth rate $*$	1.054×10^{-4}	1.054×10^{-4}	1.054×10^{-4}
r, recovery rate	1/20	1/180	1/200
ω, duration of immunity	365	274	182
d, bites per time	0.01	0.25	0.5
b, proportion of bites that lead to infection	0.2	0.35	0.5
m, mosquitoes per human	0.5	20	40
μ, mosquito mortality rate	0.275	0.275	0.275
τ, mosquito incubation period	10	10	10
v, vaccine efficacy	0	0	0

Table 5.1: Baseline parameter values for use in the SIR model by case.

Within each case, the five scenarios of varying action effectiveness are still considered: $\pm15\%$ and $\pm30\%$ intervals are once again used and are reported in Tables 5.2 and 5.3 for the optimistic and pessimistic cases, respectively. The parameter changes in the control case are the same as the ones found in Table 3.2.

Action Taken	Effect on Parameter	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
None	None	–	–	–	–	–
LLIN	$\downarrow d$	0.004564	0.005542	0.00652	0.007498	0.008476
ACT	$\uparrow r$	0.585	0.5175	0.45	0.3825	0.315
IPT	$\downarrow b$	0.098	0.119	0.14	0.161	0.182
IRS	$\downarrow m$	.1498	0.1819	0.214	0.2461	0.2782
VAC	$\uparrow v*$	0.00158	0.00144	0.00129	0.00113	0.00096

Table 5.2: These values replace the baseline parameter values if a particular action is chosen in the optimistic case. Notation: $\downarrow d$ indicates that an LLIN decreases parameter d, bites per time.

Action Taken	Effect on Parameter	Scenario 1	Scenario 2	Scenario 3	Scenario 4	Scenario 5
None	None	–	–	–	–	–
LLIN	$\downarrow d$	0.2282	0.2771	0.326	0.3749	0.4238
ACT	$\uparrow r$	0.0585	0.05175	0.045	0.03825	0.0315
IPT	$\downarrow b$	0.245	0.2975	0.35	0.4025	0.455
IRS	$\downarrow m$	11.984	14.552	17.12	19.688	22.256
VAC	$\uparrow v*$	0.00158	0.00144	0.00129	0.00113	0.00096

Table 5.3: These values replace the baseline parameter values if a particular action is chosen in the pessimistic case. Notation: $\downarrow d$ indicates that an LLIN decreases parameter d, bites per time.

5.2 Results of Parameter Variation

When running each of the three cases (pessimistic[1], control, and optimistic) with different sets of parameter values, all other factors are held constant. There are 10 rural cities each with a population of 1,000 and 1 urban city with a population of 10,000. The 11 cities share an annual budget of \$35,000/year and each city starts at population state $\begin{bmatrix} 0.50 & 0.18 & 0.32 \end{bmatrix}$. The costs of performing each action are consistent with Table 3.3. With the exception of the number of cities (cut down in this analysis due to computational complexity), these initial conditions are the same as those used in Chapter 4. The given population states assume a resolution of 0.01.

Predictably, the minimized objective values (total number of days people spend infected with malaria) differ across the three cases. Table 5.4 records the objective values (OV) in each case in each of the 5 scenarios.

The optimal intervention sequences that the ILP outputs are reported

[1]In the pessimistic case, some losses are calculated as *NaN* in MATLAB. To overcome this, we manually find and replace *NaN* losses with the average of the preceding and proceeding loss values of an entry in the output of the program int_de_script.m.

Scenario	Optimistic OV	Control OV	Pessimistic OV
1	6.33	137.90	314.2
2	7.11	766.50	345.24
3	8.13	984.88	384.98
4	9.52	1,209.26	437.54
5	11.52	1,536.40	510.72

Table 5.4: Objective values for the optimistic, control, and pessimistic cases.

in Tables 5.5, 5.6, and 5.7 for the optimistic, control, and pessimistic cases, respectively.

Scenario	No. Of Cities	Action Path	Final Destination
1, rural	3	ACT, none, none, none, none	$(1, 0)$
1, rural	7	ACT, VAC, none, none, none	$(0.99, 0)$
1, urban	1	ACT, none, none, none, none	$(1, 0)$
2, rural	10	ACT, IPT, IPT, IPT, IPT	$(1, 0)$
2, urban	1	ACT, IPT, IPT, IPT, IPT	$(1, 0)$
3, rural	10	ACT, IPT, IPT, IPT, IPT	$(1, 0)$
3, urban	1	ACT, IPT, IPT, IPT, IPT	$(1, 0)$
4, rural	10	ACT, IPT, IPT, IPT, IPT	$(1, 0)$
4, urban	1	ACT, IPT, IPT, IPT, IPT	$(1, 0)$
5, rural	10	ACT, IPT, IPT, IPT, IPT	$(1, 0)$
5, urban	1	ACT, IPT, IPT, IPT, IPT	$(1, 0)$

Table 5.5: Intervention sequences and final cell destinations in the optimistic case.

Only the ACT, IPT, VAC, and "None" actions are used throughout all three cases. While the optimistic and pessimistic cases heavily rely on IPT, the control case almost exclusively uses ACT. Vaccines are used most often in the pessimistic case–they are only used once in each of the optimistic and control cases. We also observe the largest number of unique intervention sequences in the pessimistic case.

Scenario	No. Of Cities	Action Path	Final Destination
1, rural	3	ACT, none, none, none, none	$(1, 0)$
1, rural	7	ACT, none, none, VAC, none	$(0.93, 0)$
1, urban	1	ACT, none, none, none, none	$(1, 0)$
2, rural	10	ACT, ACT, ACT, ACT, ACT	$(0.57, 0.02)$
2, urban	1	ACT, ACT, ACT, ACT, ACT	$(0.57, 0.02)$
3, rural	10	ACT, ACT, ACT, ACT, ACT	$(0.51, 0.02)$
3, urban	1	ACT, ACT, ACT, ACT, ACT	$(0.51, 0.02)$
4, rural	10	ACT, ACT, ACT, ACT, ACT	$(0.43, 0.03)$
4, urban	1	ACT, ACT, ACT, ACT, ACT	$(0.43, 0.03)$
5, rural	10	ACT, ACT, ACT, ACT, ACT	$(0.35, 0.04)$
5, urban	1	ACT, ACT, ACT, ACT, ACT	$(0.35, 0.04)$

Table 5.6: Intervention sequences and final cell destinations in the control case.

The optimistic case's objective values are consistently less than both the control and pessimistic cases, which we expect. The values also increase as scenario and pessimism of action efficacy increases. However, these values seem unrealistically low; even with interventionary action, it seems improbable that the number of days people in a malaria-endemic population spend ill can be reduced to levels as low as 6.33 over 5 years. This suggests that the most optimistic parameter values estimated in the literature may indeed be too optimistic to fit reality.

The differences in objective values in the control and pessimistic cases are somewhat counterintuitive, perhaps suggesting that some parameter variation is inconsistent with what may be truly "optimistic" and "pessimistic" in terms of the SIR model. The pessimistic case's objective value is greater than the control case's only in the first scenario. We expect the pessimistic case's objective values to be consistently greater than the control case values.

Scenario	Action Path	Final Destination	No. Of Cities
1, rural	ACT, none, none, none, none	$(1, 0)$	10
1, urban	ACT, none, none, none, none	$(1, 0)$	1
2, rural	ACT, IPT, VAC, IPT, IPT	$(1, 0)$	6
2, rural	ACT, VAC, IPT, IPT, IPT	$(1, 0)$	4
2, urban	ACT, IPT, IPT, IPT, IPT	$(1, 0)$	1
3, rural	ACT, IPT, IPT, IPT, IPT	$(1, 0)$	10
3, urban	ACT, IPT, IPT, IPT, IPT	$(1, 0)$	1
4, rural	ACT, IPT, IPT, IPT, IPT	$(1, 0)$	10
4, urban	ACT, IPT, IPT, IPT, IPT	$(1, 0)$	1
5, rural	ACT, IPT, VAC, IPT, IPT	$(1, 0)$	3
5, rural	ACT, VAC, IPT, IPT, IPT	$(1, 0)$	3
5, rural	ACT, IPT, VAC, VAC, IPT	$(0.98, 0)$	3
5, rural	ACT, VAC, IPT, VAC, IPT	$(0.98, 0)$	3
5, urban	ACT, IPT, IPT, IPT, IPT	$(1, 0)$	1

Table 5.7: Intervention sequences and final cell destinations in the pessimistic case.

The interventions chosen in scenario 1 are nearly identical in every case, but otherwise, action paths are significantly different amongst the three cases. Since scenario 1 represents the most optimistic scenario where actions are most effective, it is possible that the initial use of ACT in all three cases is effective enough to allow the "None" action in subsequent time steps.

The popular sequence in the extreme cases, ACT, IPT, IPT, IPT, IPT, suggests that ACT is used to cure the 18% of the population that is infected at $t = 1$, and then IPTs are used for the remainder of the time in order to prevent people from falling ill. This intervention schedule seems to be effective since all cities' final destinations that use this method are very close to $\begin{bmatrix} 1 & 0 & 0 \end{bmatrix}$. This action path is used exclusively in scenarios 2-5 in the optimistic case, and occasionally in the same scenarios in the pessimistic

case. The action paths that are not explicitly ACT, IPT, IPT, IPT, IPT in the pessimistic case still look similar: VAC just replaces IPT sporadically, suggesting that it is better to move the population from the S class to the R class when the threat of malaria is highest (as it is in the pessimistic case). This type of intervention schedule is not used at all in the control case.

The control case's most common action sequence, APT, APT, APT, APT, APT, takes a less proactive approach to alleviating malaria than the optimistic and pessimistic cases. Since APT acts as a cure for those who have already contracted the disease, it makes sense that there is a larger proportion of those recovered/immune in $t = 5$ in the control case than in the other cases.

Overall inconsistencies amongst the three cases in objective value and action paths implies that parameter value variation significantly affects the program's output. Since the values used come from the ranges presented in the literature, the need for more specific, reliable data becomes clear. Since the optimization of the ILP relies on the output of the SIR model, and the output of SIR model relies on specific parameter values, dependable data values are necessary to find the most realistic intervention schedules and objective values.

Chapter 6

Future Work

The malaria problem today, though inherently complex in itself, is amplified due to its concentration in developing areas with limited resources and scarce data. Due to data, model, and time constraints, the integer linear program and SIR model remain a simplistic representation of true transmission dynamics and outcomes. While the model is able to capture many aspects of the malaria problem, there are many other subtleties that could be incorporated in the future.

6.1 $SIRN$ Model

The current SIR model assumes a constant population where birth and death rates are equal, such that someone in the I class is equally as likely to die as someone in the S or R classes, and nobody dies from malaria. An SIR model that allows for varying population levels over time has been derived by Harry Dudley. He uses the ideas presented in Chitnis et al. to

amend the SIR model used in this work's analysis to account for immigration, emigration, population growth, and disease-induced death [27]. This new model is a system of four differential equations that allows for populations to change with time, but is otherwise similar to the original SIR model. A fourth class representing the population level, N, is added to the system of equations so that the three other compartments, S, I, and R, all rely on the number of people in the system. There is a distinction between the birth rate, the disease-induced death rate, and the natural death rate. Since the death rates and birth rates do not have to be equal, the population is able to vary in size over time. Dudley's system of differential equations is defined as follows:

$$\begin{aligned}
\frac{dS}{dt} &= (\frac{g}{N} + \phi)(1 - S) + \rho R - hS - vS - \delta SI \\
\frac{dI}{dt} &= hS - (\frac{g}{N} + \phi + r + \delta)I + \delta I^2 \\
\frac{dR}{dt} &= rI - (\frac{g}{N} + \rho + \phi)R + vS + \delta RI \\
\frac{dN}{dt} &= g + (\phi - f - \delta I)N,
\end{aligned}$$

where $S =$ proportion of population that is susceptible,
$I =$ proportion of population that is infected,
$R =$ proportion of population that is recovered/immune,
$\phi =$ birth rate,
$h =$ inoculation rate, defined in the same way as the constant population model,
$\rho =$ rate of immunity loss, defined in the same way as the constant population model,
$v =$ vaccine efficacy rate,
$r =$ recovery rate of infected people,
$g =$ immigration rate,
$\delta =$ malaria-induced death rate, and
$f =$ natural death rate.

Dudley assumes the baseline parameters presented in Table 6.1, based on data from Nigeria [37]. Future work would adapt our ILP framework to accommodate varying populations, using this $SIRN$ model for the population state dynamics.

6.2 Modifying the Cost Structure

The original model assumes a constant cost structure. That is to say that each intervention costs a fixed dollar amount, regardless of quantity used and varying distribution costs. Assuming fixed costs is not realistic and may therefore cause the ILP to find solutions on the basis of inaccurate data. Future work would incorporate economies of scale and differences in distribution cost.

Parameter	Baseline Value
ϕ, birth rate	1.054×10^{-4} days^{-1}
r, recovery rate	$1/180$ days^{-1}
ω, duration of immunity	274 days
d, bites per time	0.25 days^{-1}
b, proportion of bites that lead to infection	0.35 days^{-1}
m, mosquitoes per human	20
μ, mosquito mortality rate	0.275 days^{-1}
τ, mosquito incubation period	10 days
v, vaccine efficacy	0
g, (rural) immigration rate	-0.94 days^{-1}
g, (urban) immigration rate	94 days^{-1}
δ, malaria-induced death rate	8.231×10^{-6} days^{-1}
f, natural death rate	3.718×10^{-5} days^{-1}

Table 6.1: Baseline parameter values for the $SIRN$ model [37].

6.2.1 Economies of Scale

In practice, this ILP-SIR model would be most useful for philanthropic organizations planning massive intervention schemes that target entire regions. The assumption is that such organizations have a sufficient budget to interact with thousands or millions of people and households throughout the model's total time period.

Economies of scale capture the phenomenon of a decrease in price of production with an increase in quantity of a good. This decrease in price per unit is typically due to a lower average fixed cost, contributing to a lower average total cost.

This idea of decreasing prices per unit is neglected in the current cost structure. However, with the intention of providing for mass interventions, economies of scale would likely have an effect on action prices. Future

work could incorporate a linear function that better represents the costs of large quantities of anti-malaria interventions. By using a function to scale intervention prices by the total number of interventions of that type, this model can still be utilized by individuals or organizations who do not wish to perform such a large-scale intervention mission.

6.2.2 Distribution Costs

The costs of the anti-malaria interventions in the literature do not necessarily reflect the additional costs incurred by distribution. Distribution costs are especially important to consider in this model's context because malaria is primarily a problem in developing nations which lack infrastructure. Shipping and handling costs skyrocket when airports, roads, and the like are scarce. Additionally, urban cities are much more likely to have appropriate infrastructure than are rural cities. At the moment, the costs for each action is the same regardless of region. Future work would better estimate the costs of distribution for the different interventions for each region.

6.3 Concluding Remarks

In this thesis, we refine the work of Hoeger et al. by improving population state resolution and conducting sensitivity analysis on model parameters [22]. In Chapter 4, we find that changing the resolution produces differences in the ILP's objective value and intervention schedules. We also find that varying parameter values greatly affects objective values and alters action paths, as discussed in Chapter 5. This suggests that the ILP and

SIR frameworks are sensitive to changes in resolution and the literature-reported ranges of parameter values.

Consistent with the literature, ACT and IPT appear to be the most cost-effective interventions since they are included in most action sequences. Although the model itself would benefit from the relaxation of certain assumptions, its time-dynamic methodologies can be useful for policy makers and health organizations looking to eradicate malaria in developing areas.

Appendix A

Program Code

The appendix includes the code necessary to run the optimization model. This code was originally written by Hoeger et al. and is adapted to fit the refinements made in this thesis [22]. The program utilizes MATLAB, Python, and AMPL, which is then input into the NEOS Solver online (http://www.neos-server.org/neos/). Although I use Gurobi for all analysis, a future user may use any solver that reads the AMPL language.

A.1 MATLAB Code

The portion of the code written in MATLAB generates the bulk of the program's data. The MATLAB code generates population states given a resolution, solves the SIR model, and calculates losses for each population state given action, region, and scenario.

A.1.1 Helper Functions

The following "helper functions" are called upon in the data-generating programs.

sir_de.m

sir_de.m is the SIR system of differential equations.

```
% sir_de.m
% evaluates derivatives at the given IC

function dxdt=sir_de(x,phi,q,omega,a,b,m,mu,tau,v)
S=x(1); I=x(2); R=x(3);
h=m*b*a^2*exp(-mu*tau)*I/(mu+a*b*I);
rho=((h+phi)*exp(-(h+phi)*omega))/(1-exp(-(h+phi)*
   omega));
dxdt=[phi - phi*S - h*S + rho*R - v*S
     h*S - (q + phi)*I
     q*I - (rho + phi)*R + v*S];
return
```

genPopVec.m

genPopVec.m generates the population vectors given a user-inputted resolution.

```
% generate population vectors

function pStates=genPopVec(res)
% res=population resolution

    N=(1+(1/res+1))*(1/res+1)/2; % calculate total
       number of states

    pStates=zeros(3,N);
```

```
    count=1;

    while count<N
        for i=0:(1/res)
            for j=0:(1/res-i)
                k=1/res-i-j;
                pStates(:,count)=[i;j;k]*res; % divide
                    by 1/res to scale to %ages
                count=count+1;
            end
        end
    end

return
```

round2.m

round2.m is the rounding function described in Chapter 4.

```
function output=round2(vec,res)
% input: pop. vector vec and vector resolution res
% output: rounded pop. vector

default=round(vec/res)*res; % round normally
% nextDec=mod(vec,res); % extract 2nd decimal place
diff=sum(default)-1; % check sum of components

if diff==0 % if sum = 1, do nothing
    output=default;
else % adjust # with smallest % error
    [~,ind]=max(vec); % take largest compartment
    default(ind)=default(ind)-diff;
    output=default;
end
return
```

FJ2012_findSubInd.m

FJ2012_findSubInd.m indexes SIR population states for use in data processing.

```
function subInd = FJ2012_findSubInd (SI, in)
% function: re-label the population state
% input: SI:    two columns for S and I in population state
%        in:    increment in population
% output: (m, n) indicating the subscript indices of the population state
% date: 2012/07/26
% author: FX

spVec = linspace(0, 1, 1/in+1);     %
dim = length(spVec);                % dimension of the population states

% initialize the individual indices
m = 0;                              % row index: S
n = 0;                              % col index: I

% initialize the matrix of indices
subInd = [];
SI = round(SI.*100)/100;            % fix some rounding problem
[row col] = size(SI);
for i = 1:row
    m = dim + 1 - find(spVec == SI(i,1));
    n = find(spVec == SI(i,2));
    subInd = [subInd; m n];
end
```

A.2 Calculation Scripts

The following two MATLAB scripts calculate the bulk of the data for the program.

paramScriptScen.m

paramScriptScen.m generates the transitions from population state to population state by numerically solving the SIR model for every action and scenario. It outputs one .xls file per scenario (5 .xls files per single run) that is later used in the Python program to be translated into an AMPL format. The .xls files are headerless, but can be organized into the following columns: initial S, initial I, next S, next I, action #, scenario #.

```
1  % produces 5 .xls files, one for each scenario
2
3  tic
4  %% Generate population vectors
5  res=.01; % resolution of population vectors
6
7  popStates=genPopVec(res);
8  N=length(popStates); % count number of population
       vectors
9
10
11 %% Define baseline parameters
12 % time units in DAYS
13 phi=1.054e-4; % birth/death rate
14 r=1/180;      % recovery rate
15 omega=274;    % duration of immunity
16 d=.25;        % bites per time
17 b=.35;        % proportion of bites that lead to
       infection
18 m=20;         % mosquitos per human
19 mu=.275;      % mosquito mortality rate
20 tau=10;       % incubation period
21 v=0;          % vaccine efficacy
22
```

```
23 base=[phi r omega d b m mu tau v]; %base=baseline
      parameters
24
25 %% Set up actions
26 %base=[delta r omega a b m mu tau v];
27 scen=(1:5)';
28
29 LLINa=[0.114, 0.139, 0.163, 0.187, 0.212]';
30 LLIN=[1*ones(5,1) scen repmat(base(1:3),5,1) LLINa
      repmat(base(5:9),5,1)];
31
32 ACTr=[.065, .058, .05, .043, .035]';
33 ACT=[2*ones(5,1) scen repmat(base(1),5,1) ACTr repmat(
      base(3:9),5,1)];
34
35 IPTb=[0.172, 0.208, 0.245, 0.282, 0.319]';
36 IPT=[3*ones(5,1) scen repmat(base(1:4),5,1) IPTb
      repmat(base(6:9),5,1)];
37
38 IRSm=[5.99, 7.28, 8.56, 9.84, 11.13]';
39 IRS=[4*ones(5,1) scen repmat(base(1:5),5,1) IRSm
      repmat(base(7:9),5,1)];
40
41 Vac_yearly=[0.78, 0.69, 0.60, 0.51, 0.42]';
42 Vacv=(1+Vac_yearly).^(1/365)-1;
43 Vac=[5*ones(5,1) scen repmat(base(1:8),5,1) Vacv];
44
45 % matrix where each row is in the format [scenario#
      action# parameters]
46 actions=[zeros(5,1) scen repmat(base,5,1); % a0: do
      nothing
47          LLIN; ACT; IPT; IRS; Vac];
48
49
50 %% Create files
51
52 % generate filename according to date/time
53 filename=cell(1,5);
54 date=datestr(now,'mmddyy_HHMM_');
55 for i=1:5
```

```
56      filename{i}=[date 'sc' num2str(i) '.xls'];
57  end
58
59  %% Loop over all actions
60
61  for X=1:length(actions)
62      p=actions(X,:);
63      disp(p(1:2)) % display action & scen # (for
            tracking script progress)
64      sceNum=p(2); % extract scenario number
65
66      if actions(X,1)==0 && actions(X,2)>1
67          % if on action 0 and not 1st scen., skip
                calculation
68          % and write previous result to file
69          dlmwrite(filename{sceNum},mat,'delimiter','\t
                ','-append');
70      else
71          % function handle for solving with ode45
72          % de=@(t,x) sir_de(x,phi,r,omega,a,b,m,mu,tau,
                v);
73          de=@(t,x) sir_de(x,p(3),p(4),p(5),p(6),p(7),p
                (8),p(9),p(10),p(11));
74
75          next=zeros(3,N);
76          for i=1:N % loop over all pop states
77              sol=ode45(de,[0,365],popStates(:,i)); %
                    solve with initial condition
78              pop=deval(sol,365,1:3); % evaluate at t
                    =365 days
79              next(:,i)=round2(pop,res); % use rounding
                    helper function
80          end
81
82          % save data for all pop states
83          mat=[popStates;next;repmat(p',1,N)]'; % matrix
                of initial and final pop states
84          matSmall=[mat(:,1:2) mat(:,4:5) mat(:,7:8)];
85
86          % write data to Excel file
```

```
87          dlmwrite(filename{sceNum},matSmall,'delimiter
               ','\t','-append');
88      end
89  end
90      toc
```

int_de_script.m

int_de_script.m calculates the losses associated with performing different actions in different scenarios, regions, and population states. It outputs 5 .xls files, one for each scenario. The .xls files are headerless, but can be organized into the following columns: initial S, initial I, action #, region, loss.

```
1  % use this file to generate rewards for each pop state
      /action/
2  % region combo. Losses are based on numerical
      integration of
3  % the infected curve of the SIR model solution for
      each popstate.
4
5  tic
6  %% Generate population vectors
7  res=.01; % resolution of population vectors
8
9  popStates=genPopVec(res);
10 N=length(popStates); % count number of population
      vectors
11
12 %% Define region populations
13 regPops=[1 10]'; % ****in THOUSANDS of people***
14 R=length(regPops); % number of regions
15 Rind=(1:R)';
16
17 %% Define baseline parameters
18 phi=1.054e-4; % birth/death rate
19 r=1/180;      % recovery rate
20 omega=274;    % duration of immunity
```

```
d=.25;          % bites per time
b=.35;          % proportion of bites that lead to
   infection
m=20;           % mosquitos per human
mu=.275;        % mosquito mortality rate
tau=10;         % incubation period
v=0;            % vaccine efficacy

base=[phi r omega d b m mu tau v]; %base=baseline
   parameters

%% Set up actions
%base=[phi r omega a b m mu tau v];
scen=(1:5)';

LLINa=[0.114, 0.139, 0.163, 0.187, 0.212]';
LLIN=[1*ones(5,1) scen repmat(base(1:3),5,1) LLINa
   repmat(base(5:9),5,1)];

ACTr=[.065, .058, .05, .043, .035]';
ACT=[2*ones(5,1) scen repmat(base(1),5,1) ACTr repmat(
   base(3:9),5,1)];

IPTb=[0.172, 0.208, 0.245, 0.282, 0.319]';
IPT=[3*ones(5,1) scen repmat(base(1:4),5,1) IPTb
   repmat(base(6:9),5,1)];

IRSm=[5.99, 7.28, 8.56, 9.84, 11.13]';
IRS=[4*ones(5,1) scen repmat(base(1:5),5,1) IRSm
   repmat(base(7:9),5,1)];

Vac_yearly=[0.78, 0.69, 0.60, 0.51, 0.42]';
Vacv=(1+Vac_yearly).^(1/365)-1;
Vac=[5*ones(5,1) scen repmat(base(1:8),5,1) Vacv];

% matrix where each row is in the format [scenario#
   action# parameters]

actions=[zeros(5,1) scen repmat(base,5,1); % a0: do
   nothing
```

```
53          LLIN; ACT; IPT; IRS; Vac];
54
55  %% Create files
56
57  % generate filename according to date/time
58  filename=cell(1,5);
59  date=datestr(now,'mmddyy_HHMM_');
60  for i=1:5
61      filename{i}=[date 'rewards_sc' num2str(i) '.xls'];
62  end
63
64  %% Loop over all actions
65
66  for X=1:length(actions)
67      p=actions(X,:);
68      disp(p(1:2)) % display action & scen # (for
           tracking script progress)
69      sceNum=p(2); % extract scenario number
70
71      if actions(X,1)==0 && actions(X,2)>1
72          % if on action 0 and not 1st scen., skip
               calculation
73          % and write previous result to file
74          dlmwrite(filename{sceNum},mat,'delimiter','\t
               ','-append');
75      else
76          % function handle for solving with ode45
77          % de=@(t,x) sir_de(x,phi,r,omega,a,b,m,mu,tau,
               v);
78          de=@(t,x) sir_de(x,p(3),p(4),p(5),p(6),p(7),p
               (8),p(9),p(10),p(11));
79
80          % initialize data table: initS, initI, action,
                region, loss
81          mat=zeros(N*R,5);
82
83          for i=1:N % loop over all popStates
84              sol=ode45(de,[0,365],popStates(:,i)); %
                   solve with initial condition
85              t = 0:365;
```

```
86              in = deval(sol,t,2); % extract infected %
                   from DE soln
87              nin = zeros(1,length(in)-1);
88              for j=1:length(nin)
89                  nin(j) = (in(j)+in(j+1))/2; % create a
                        midpoint summation to approximate
                       reward
90              end
91              idays = sum(nin);
92              ippldays = idays*regPops; % convert
                   percentage to # of people
93              mat((R*(i-1)+1):R*i, :) = ...
94                  [repmat([popStates(1:2,i)' p(1)],R,1)
                       Rind ippldays];
95          end
96
97      % write data to Excel file
98      dlmwrite(filename{sceNum},mat,'delimiter','\t','-
           append');
99      end
100 end
101
102 toc
```

A.3 Data Processing Programs

The following two functions reformat the .xls output of paramScriptScen.m and int_de_script.m for use in the Python program.

FJ2012_DatToAmpl.m

FJ2012_DatToAmpl.m uses the .xls files created by paramScriptScen.m to produce two .mat files (per single .xls file) conveying information about the transitions from population state to population state given actions and initial population states.

```
function FJ2012_DatToAmpl(filename, scenario)
tic
% function: process the raw data into datasets that
   will be used as input
% in Python for AMPL
% Input:    filename: .xls files from paramScriptScen.
   m
%           scenario: index of scenario, ranging in
   1...5
% Output:   ActOut, indexed by ((m,n), action)
%           ActIn, indexed by ((m,n), (j,k), action)
% date: 2012/07/27
% author: FX

%% parameter setting
in = 0.01; % increment in pop states

% load the whole dataset
dataSet = dlmread(filename, '\t');
% locate the specific scenario
sce = dataSet(:, 6);                % col F
sceInd = find(sce == scenario);

% S & I of initial pop states (m, n)
iniSI = dataSet(sceInd, 1:2);
% S & I of endOfYear pop states (j, k)
endSI = dataSet(sceInd, 3:4);
% the corresponding actions from (m, n) -> (j, k)
act = dataSet(sceInd,5);

%% re-labeling the pop state
iniPS = FJ2012_findSubInd(iniSI, in);
endPS = FJ2012_findSubInd(endSI, in);
% total number of actions
[N dum] = size(iniPS);

%% Action Set
% define a cell of actions
actSet = {'none'; 'LLIN'; 'ACT'; 'IPT'; 'IRS'; 'VAC
```

```
   ';};
% number of distinctive actions
nAct = length(actSet);
% create index for corresponding action
indAct = [1:nAct]';

%% ActOut(statePosAct)

[ActOut distIniPS nDistIniPS] = ActInOrOut(iniPS, act,
    indAct);
cellActOut = outputInCell(ActOut, distIniPS,
   nDistIniPS, actSet);
fileN = [filename, 'cellActOut.mat'];
save(fileN, 'cellActOut');

%% ActIn (stateInPosAct)
[ActIn dist nDist] = ActInOrOut([iniPS endPS], act,
   indAct);
cellActIn = outputInCell(ActIn, dist, nDist, actSet);
fileN = [filename, 'cellActIn.mat'];
save(fileN, 'cellActIn');


%% Return a column indicating whether an action could
   be taken for each
%% tuple, either action out (m, n), or action in
   indexed by ((m, n), (j, k))
    function [ACT distRawData nDistRawData] =
       ActInOrOut(rawData, act, indAct)
    % Input:    rawData:        matrix of (m, n) or (m
       , n, j, k)
    %           act:            all actions based on
       the rawData
    %           indAct:         [1 2 3 4 5 6]'
    % Output:   ACT:            a matrix contains
       possible actions taken
    %                           for each population
       state (m, n)
    %           distRawData:    distinctive tuples in
       rawData
```

```
65      %           nDistRawData:   number of distinctive
           tuples
66      distRawData = unique(rawData, 'rows');
67      nDistRawData = length(distRawData);
68      ACT = [];
69      ACTVal = [];
70      for j = 1:nDistRawData
71          loc = ismember(rawData, distRawData(j, :), '
               rows');
72          indLoc = find(loc == 1);
73          indvAct = act(indLoc);
74          ACTVal = ismember(indAct,(indvAct+1)).*indAct;
75          ACT = [ACT; ACTVal];
76      end
77      end
78
79  %% Return a cell containing the following information:
80  %%      ActOut: row structure is [m, n, action i,
       action indicator]
81  %%              action i can be taken from pop state (
       m, n) then action
82  %%              indicator = the index of this action,
       otherwise, set it 0.
83  %%      ActIn:  row structure is [m, n, j, k, action i
       , action indicator]
84  %%              action i can be taken from pop state (
       m, n) to pop state
85  %%              (j, k) then action indicator = the
       index of this action;
86  %%              otherwise set it 0.
87      function cellACT = outputInCell(ACT, distRawData,
           nDistRawData, actSet)
88          % Input:  ACT:          action indictors
89          %         disRawData:   distinctive tuples in
               rawData
90          %         nDistRawData: number of distinctive
               tuples
91          %         actSet:       {'none'; 'LLIN'; 'ACT
               '; 'IPT'; 'IRS'; 'VAC'}
92          % Output: cellACT
```

```
93          nAct = length(actSet);
94          body = kron(distRawData, ones(nAct, 1));
95          cellBody = num2cell(body);
96          cellACT = [cellBody repmat(actSet,
               nDistRawData,1) num2cell(ACT)];
97      end
98  toc
99  end
```

FJ2012_LossToAmpl.m

FJ2012_LossToAmpl.m uses the .xls files created by int_de_script.m to produce .mat files that translate region and action numbers to strings. The contents of these .mat files must be copied and pasted over the original .xls files created by int_de_script.m to be compatible with the Python program.

```
1  function [] = FJ2012_LossToAmpl()
2  %scripts to process the Loss data
3  tic
4  %% parameter setting
5  in = 0.01;              % increment in pop states
6
7  % load the whole dataset
8  dataSet = dlmread('022013_2340_rewards_sc5.xls');
9  % S & I of initial pop states (m, n)
10 SI = dataSet(:, 1:2);
11 % the actions from (m, n)
12 act = dataSet(:,3);
13 % region codes
14 reg = dataSet(:, 4);
15 % loss for each pop state and each action of each
      region
16 loss = dataSet(:, 5);
17
18 %% re-labelling the pop-state
19 PS = FJ2012_findSubInd(SI, in);
```

```
20
21 %% Action Set
22 % define a cell of actions
23 actSet = {'none'; 'LLIN'; 'ACT'; 'IPT'; 'IRS'; 'VAC
       ';};
24 % number of distinctive actions
25 nAct = length(actSet);
26 % create index for corresponding action
27 indAct = [1:nAct]';
28
29 %% Region Set
30 % define a cell of regions
31 regSet = {'rural'; 'urban';};
32 % number of distinctive regions
33 nReg = length(regSet);
34 % create index for corresponding action
35 indReg = [1:nReg]';
36
37 %% replace the code with words
38 opAct = code2words((act+1), actSet, nAct, indAct);
39 opReg = code2words(reg, regSet, nReg, indReg);
40
41 %% output the whole dateset
42 cellLoss = [num2cell(PS) opAct opReg num2cell(loss)];
43 fileN = ['cellLoss05.mat'];
44 save(fileN, 'cellLoss');
45
46
47
48 function outPut = code2words(DS, set, nSet, indSet)
49 outPut = cell(size(DS));
50 for i = 1:nSet
51     loc = ismember(DS, indSet(i));
52     indLoc = find(loc == 1);
53     outPut(indLoc) = {set(i)};
54 end
55 toc
```

A.4 Python Code

The MATLAB output (.xls and .mat files) is used by the single Python program, datForAMPL_difnumcities.py, that converts the inputted data into a data file in the AMPL language (.dat). This program must be run once for each scenario.

Explicitly, datForAMPL_difnumcities.py uses 4 .xls files, 3 of which are created by hand, and the 2 .mat files outputted by FJ2012_DatToAmpl.m. The costs and budgets file, as well as the two (one for each region) initial population files are created by hand.

datForAMPL_difnumcities.py

```
1  # Input Data Ampl
2  # Based off of ampldataNVersion.dat
3  """ We wish to take information from excel data sheets
       and output ampl
4          datasheets.
5
6          This is meant to match the format of ampldata
              sheet InOut_Act5_PSdim5_txt.'
7
8          This data sheet needs the many files under
              Matrices and Excel Input
9          Files to run correctly.
10
11  Imports
12 """
13 import scipy.io
14 import random
15 import math
16 from numpy import *
17 from xlrd import open_workbook, XL_CELL_TEXT
```

```
18 import unicodedata
19
20 """
21 Matrices and Excel Input Files
22 """
23 # Costs and Simple Inputs
24 book = open_workbook('073012_costs.xls') # Ex. excel
25 simpleInputs = book.sheet_by_index(1)
26 costS = book.sheet_by_index(0)
27 # Initial Rural Population States
28 iniPop_r = open_workbook('InitialPop_02.xls')
29 sheet1 = iniPop_r.sheet_by_index(0)
30 sheet2 = iniPop_r.sheet_by_index(1)
31 # Initial Urban Population States
32 iniPop_u = open_workbook('InitialPop_02.xls')
33 sheet3 = iniPop_u.sheet_by_index(2)
34 sheet4 = iniPop_u.sheet_by_index(3)
35 # actionsOut
36 aOut1 = scipy.io.loadmat('021913_1629_sc5.
      xlscellActOut.mat')
37 aOut = aOut1['cellActOut']
38 # actionsIn
39 aIn1 = scipy.io.loadmat('021913_1629_sc5.xlscellActIn.
      mat')
40 aIn = aIn1['cellActIn']
41
42 # loss
43 R = open_workbook('021913_1611_rewards_sc5.xls')
44 rSht2 = R.sheet_by_index(0)
45
46
47
48 """
49  Helpers
50 """
51
52 def makeList():
53         alist = raw_input("# Enter a list: ").strip()
54         if not alist.startswith('[') or not alist.
             endswith(']'):
```

```
55                print "# ERROR!"
56                return None
57        return eval(alist)
58 # process found at http://www.daniweb.com/software-
      development/python/threads/107239/list-input on
      july 18, 2012
59
60
61 """
62 #Begin Process
63 """
64 # time steps
65 thyme = simpleInputs.cell_value(0,3)
66 time = int(thyme)
67
68 # Cost
69 cost = ''
70 for i in range(1, costS.nrows):
71         if costS.cell_value(i, 0) == 0 and costS.
             cell_value(i,1) == 1:
72                 value = costS.cell_value(i, 2)
73                 cost += 'none ' +  str(value)
74         elif costS.cell_value(i, 0) == 0 and costS.
             cell_value(i,1) == 2:
75                 value = costS.cell_value(i, 2)
76                 cost += ' ' +  str(value) + ' \n'
77         elif costS.cell_value(i, 0) == 1 and costS.
             cell_value(i,1) == 1:
78                 value = costS.cell_value(i, 2)
79                 cost += 'LLIN ' +  str(value)
80         elif costS.cell_value(i, 0) == 1 and costS.
             cell_value(i,1) == 2:
81                 value = costS.cell_value(i, 2)
82                 cost += ' ' +  str(value) + ' \n'
83         elif costS.cell_value(i, 0) == 2 and costS.
             cell_value(i,1) == 1:
84                 value = costS.cell_value(i, 2)
85                 cost += 'ACT ' +  str(value)
86         elif costS.cell_value(i, 0) == 2 and costS.
             cell_value(i,1) == 2:
```

```
87                  value = costS.cell_value(i, 2)
88                  cost += ' ' +  str(value) + ' \n'
89          elif costS.cell_value(i, 0) == 3 and costS.
               cell_value(i,1) == 1:
90                  value = costS.cell_value(i, 2)
91                  cost += 'IPT ' +  str(value)
92          elif costS.cell_value(i, 0) == 3 and costS.
               cell_value(i,1) == 2:
93                  value = costS.cell_value(i, 2)
94                  cost += ' ' +  str(value) + ' \n'
95          elif costS.cell_value(i, 0) == 4 and costS.
               cell_value(i,1) == 1:
96                  value = costS.cell_value(i, 2)
97                  cost += 'IRS ' +  str(value)
98          elif costS.cell_value(i, 0) == 4 and costS.
               cell_value(i,1) == 2:
99                  value = costS.cell_value(i, 2)
100                 cost += ' ' +  str(value) + ' \n'
101         elif costS.cell_value(i, 0) == 5 and costS.
               cell_value(i,1) == 1:
102                 value = costS.cell_value(i, 2)
103                 cost += 'VAC ' +  str(value)
104         elif costS.cell_value(i, 0) == 5 and costS.
               cell_value(i,1) == 2:
105                 value = costS.cell_value(i, 2)
106                 cost += ' ' +  str(value) + ' \n'
107
108
109
110
111
112 # Geographic regions
113 geoReg = ''
114 regionL= simpleInputs.row_values(1,0) #List of regions
115 for i in range(1,len(regionL)):
116         if regionL[i] == '':
117                 geoReg += ''
118         else:
119                 value = simpleInputs.cell_value(1,i)
120                 geoReg +=" '" +value +"'"
```

```
121
122 # Action Sets
123 actSet = ''
124 actA = simpleInputs.row_values(2,0) #List of actions
125 for i in range(1,len(actA)):
126         if actA[i] == '':
127                 actSet += ''
128         else:
129                 value = simpleInputs.cell_value(2,i)
130                 actSet += " '" + value + "'"
131
132 # Budget
133 budget = ''
134 B = simpleInputs.row_values(3,0)
135 for i in range(1,len(B)):
136         if B[i] == '':
137                 budget += ''
138         else:
139               value = simpleInputs.cell_value(3,i)
140               budget += str(i) + ' ' + str(value) + '
                    '
141
142
143 # DimRow & dimCol
144 dim = sheet1.cell_value(2,5)
145 dimRow = int(dim)
146 dimCol = int(dim)
147
148 # big N
149 totPop = sheet1.cell_value(0,5)+1
150 N = int(totPop)
151
152 # initial rural and urban populations
153 ini_r = ''
154 for i in range(1, sheet2.nrows):
155         for j in range(0, sheet2.ncols):
156                 value1 = sheet2.cell_value(i,j)
157                 intVal1 = int(value1)
158                 ini_r += str(intVal1) + ' '
159         value2 = sheet4.cell_value(i,2)
```

```
160         intVal2 = int(value2)
161         ini_r += str(intVal2) + ' '
162         ini_r += ' \n'
163 
164 # initial urban population
165 ##ini_u = ''
166 ##for i in range(1, sheet4.nrows):
167 ##         for j in range(2, sheet4.ncols):
168 ##                 value = sheet4.cell_value(i,j)
169 ##                 intVal = int(value)
170 ##                 ini_u += str(intVal) + ' '
171 ##         ini_u += ' \n'
172 
173 # loss
174 loss = ''
175 for i in range(0,rSht2.nrows):
176         for j in range(0, 2):
177                 value = rSht2.cell_value(i,j)
178                 intVal = int(value)
179                 loss += str(intVal) + ' '
180         for j in range(2, rSht2.ncols):
181                 value = rSht2.cell_value(i,j)
182                 loss += str(value) + ' '
183         loss += ' \n'
184 
185 
186 
187 """
188 Start Output String
189 """
190 allText=[]
191 
192 #---------- Data to be copied directly into AMPL files
193 allText.append("param T := " +str(time) + " ; \n")
194 allText.append("param N := " + str(N) + " ; \n")
195 allText.append("set Georeg := " + geoReg + " ; \n" )
196 allText.append("param bud := " + budget + " ; \n")
197 allText.append("param dimRow:= " + str(dimRow) + " ; \
    n")
```

```
198 allText.append("param dimCol:= " + str(dimCol) + " ; \
       n")
199 allText.append("param: statePos: initialp_r initialp_u
       := \n" + ini_r + " ; \n")
200 #allText.append("param: statePos: initialp_u := \n" +
       ini_u + " ; \n")
201 allText.append("set Actioni := " + actSet + " ; \n")
202 allText.append("param actionCost: \n   rural urban :=
       \n" + cost + " ; \n")
203 allText.append("param: statePosActReg: loss := \n " +
       loss + " ; \n")
204
205 # ActionOut
206 allText.append( "param: statePosAct: ActOut := \n")
207 for i in range(aOut.shape[0]):                # for
       full height... for i
208 #for i in range(0,19):                          # the
        height of aOut
209         initStr= ''
210         # For full width
211         for j in range(aOut.shape[1]):          #
              width
212               cell = aOut[i,j]
213               if j==2:                          # make
                   the bracketed text-strings into
                  strings
214                     noUni = unicodedata.normalize
                           ('NFKD',cell[0]).encode('
                          ascii','ignore')
215                     initStr = initStr + noUni + '
                           '
216               else:                             # make
                   the double-bracketed ints into
                  strings
217                     getInt = cell[0,0]
218                     initStr = initStr +  str(
                          getInt) +'  '
219         allText.append( initStr)
220 allText.append(' ; \n')
221
```

```
222 # ActionIn
223 allText.append( "param: stateInPosAct: ActIn := \n")
224 for i in range(aIn.shape[0]):
225 #for i in range(0,19):                              # the
        height of aIn
226         initStr= ''
227         # For full width
228         for j in range(aIn.shape[1]):           # width
229                 cell = aIn[i,j]
230                 if j==4:                            # make
                        the bracketed text-strings into
                       strings
231                         noUni = unicodedata.normalize
                           ('NFKD',cell[0]).encode('
                           ascii','ignore')
232                         initStr = initStr + noUni + '
                             '
233                 else:                               # make
                        the double-bracketed ints into
                       strings
234                         getInt = cell[0,0]
235                         initStr = initStr +  str(
                           getInt) +'  '
236         allText.append( initStr)
237 allText.append(' ; \n')
238
239 #---------- Assign filename & create file
240 filename=str(raw_input('Enter a filename + file
       extension (ex. george.dat)'))
241 f = open(filename, 'w')
242
243 for i in range(len(allText)):                       #
       create file
244     f.write('\n'+allText[i])
245
246 f.close()
247 print "Done! Data written to " + filename
248
249 """
```

```
250 It may behove future researchers to make the loops
       more efficient.
251 """
```

A.5 AMPL Code

The NEOS Solver can solve a linear programming problem coded in AMPL with three separate files: model, data, and run. Only the data file, output by datForAMPL_difnumcities.py, changes throughout the analysis in this thesis.

RUNNING_h.mod

RUNNING_h.mod is the model file for the optimization program. It defines the integer linear program, including its parameters and constraints.

```
1  /*
2  3-dimensional population states
3   */
4
5  param T >=0;                              # End time
       step
6  param N >=0;                              # Big N >
       total population
7  param dimRow >=0;                         # Dimension of
        population states
8  param dimCol >=0;                         # determined
       by increment
9
10 set Georeg;                               # Geographical
        Region Set
11 set Actioni;                              # Action Set
12
13 set statePos within {1..dimRow, 1..dimCol};
              # Pop state position
```

```
14 set statePosAct within {statePos, Actioni} ;
15 set stateInPosAct within {statePos, statePosAct} ;
16 set statePosActReg within {statePosAct, Georeg};
17
18 param ActIn{stateInPosAct} >= 0 ;
19 param ActOut{statePosAct} >= 0 ;
20
21 # initial population states
22 param initialp_r{statePos} >= 0;
23 param initialp_u{statePos} >= 0;
24
25 # budget in a timestep must be positive
26 param bud{t in 1..T} >= 0;
27
28 # cost per action taken in region g
29 param actionCost{i in Actioni, g in Georeg} >= 0;
30
31 # loss per action taken in population state p_jk of
      region g
32 param loss{statePosActReg} >=0;
33
34 # Number of cells in population state p_jk in region g
       at time t, ghost time T+1
35 var Pjkgt {statePos, g in Georeg, t in 1..T} integer
      >= 0;
36
37 # Number of cells in state (m,n) into state (j,k)  of
      region g,
38 # taking IN action i  at time t
39 var aINmnjklgt {stateInPosAct, g in Georeg, t in 1..T}
       integer >= 0;
40 var aOUTjklgt {statePosAct, g in Georeg, t in 1..T}
      integer >= 0;
41
42
43 minimize totLoss:
44 sum{t in 1..(T-1), (j,k,l) in statePosAct, g in Georeg
      }
45 (loss[j,k,l,g]*aOUTjklgt[j,k,l,g,t]);
46
```

```
47 subject to budget_constraint {t in 1..T}:
48 sum{l in Actioni, g in Georeg}
49 (actionCost[l,g]*(sum{(j, k) in statePos}(aOUTjklgt[j,
      k,l,g,t]))) <= bud[t];
50
51 subject to initial_pop1_r {(j, k) in statePos, g in
      Georeg:g=='rural'}:
52 Pjkgt[j,k,g,1] = initialp_r[j,k];
53 subject to initial_pop1_u {(j, k) in statePos, g in
      Georeg:g=='urban'}:
54 Pjkgt[j,k,g,1] = initialp_u[j,k];
55
56 subject to popConserv {g in Georeg, t in 1..T-1}:
57 sum{(j, k) in statePos} (Pjkgt[j,k,g,t]) = sum {(j, k)
       in statePos} (Pjkgt[j,k,g,t+1]) ;
58
59 subject to actOutTot {(j,k) in statePos, g in Georeg,
      t in 1..T}:
60 sum{l in Actioni: (j,k,l) in statePosAct} (aOUTjklgt[j
      ,k,l,g,t]) = Pjkgt[j,k,g,t] ;
61
62 subject to flow_balance {(j, k) in statePos, g in
      Georeg, t in 1..T-1 }:
63 Pjkgt[j,k,g,t]
64 + sum{l in Actioni, (m, n) in statePos: (m,n,j,k,l) in
       stateInPosAct} (aINmnjklgt[m,n,j,k,l,g,t])
65 - sum{l in Actioni} (aOUTjklgt[j,k,l,g,t])
66 = Pjkgt[j,k,g,t+1];
67
68 # taking out those actions which do not exist
69 subject to ghostIN {(m,n,j,k,l) in stateInPosAct, g in
       Georeg, t in 1..T} :
70 aINmnjklgt[m,n,j,k,l,g,t] <= N*ActIn[m,n,j,k,l] ;
71 subject to ghostOUT {(j,k,l) in statePosAct, g in
      Georeg, t in 1..T} :
72 aOUTjklgt[j,k,l,g,t] <= N*ActOut[j,k,l] ;
73
74 # connecting in and out
75 subject to inNOut {(m, n) in statePos, l in Actioni, g
       in Georeg, t in 1..T} :
```

```
76 sum{(j, k) in statePos: (m,n,j,k,l) in stateInPosAct }
       (aINmnjklgt[m,n,j,k,l,g,t])
77 = aOUTjklgt[m,n,l,g,t] ;
```

RUNNINGList.run

RUNNINGList.run tells the NEOS Solver what to display to its user. This particular file was given to Hoeger et al. by Professor Martonosi of Harvey Mudd College and only displays variables that are positive.

```
1  # AMPL options file--exactly the same as Prof.
       Martonosi's Lecture3ex.run file
2
3  # This file is used to specify options to AMPL when
       running a "full" solution (i.e. from solve.sh)
4
5  # Send the model to AMPL
6  solve;
7
8  # Save output:
9  # Store only those variables that are positive
10
11 display {j in 1.._nvars: _var[j]>0} (_varname[j],_var[
       j]);
12
13 option omit_zero_rows 1; # set option to 1
```

Sample .dat File

Below is a sample of the direct output of datForAMPL_difnumcities.py to be used as the AMPL data file. One .dat file is needed per scenario. This particular sample comes from scenario 1 of the control case.

```
param T := 6 ;

param N := 11 ;
```

```
set Georeg :=  'rural' 'urban' ;

param bud := 1 35.0 2 35.0 3 35.0 4 35.0 5 35.0 6 35.0  ;

param dimRow:= 101 ;

param dimCol:= 101 ;

param: statePos: initialp_r initialp_u:=
1 1 0 0
2 1 0 0
2 2 0 0
3 1 0 0
3 2 0 0
3 3 0 0
4 1 0 0
4 2 0 0
4 3 0 0
4 4 0 0

⋮

101 101 0 0
 ;

set Actioni :=  'none' 'LLIN' 'ACT' 'IPT' 'IRS' 'VAC' ;

param actionCost:
   rural urban :=
none 0.0 0.0
LLIN 1.17 11.7
ACT 0.67 6.7
IPT 0.18 1.8
IRS 1.08 10.8
VAC 5.0 50.0
 ;

param: statePosActReg: loss :=
 101 1 'none' 'rural' 0.0
101 1 'none' 'urban' 0.0
```

```
101 2 'none' 'rural' 39.889
101 2 'none' 'urban' 398.89
101 3 'none' 'rural' 37.551
101 3 'none' 'urban' 375.51

⋮

1 1 'none' 'urban' 0.0
101 1 'LLIN' 'rural' 0.0
101 1 'LLIN' 'urban' 0.0

⋮

1 1 'LLIN' 'urban' 0.0
101 1 'ACT' 'rural' 0.0
101 1 'ACT' 'urban' 0.0

⋮

1 1 'ACT' 'urban' 0.0
101 1 'IPT' 'rural' 0.0
101 1 'IPT' 'urban' 0.0

⋮

1 1 'IPT' 'urban' 0.0
101 1 'IRS' 'rural' 0.0
101 1 'IRS' 'urban' 0.0

⋮

1 1 'IRS' 'urban' 0.0
101 1 'VAC' 'rural' 0.0
101 1 'VAC' 'urban' 0.0

⋮

1 1 'VAC' 'urban' 0.0
 ;

param: statePosAct: ActOut :=
```

```
1  1  none  1
1  1  LLIN  2
1  1  ACT  3
1  1  IPT  4
1  1  IRS  5
1  1  VAC  6
2  1  none  1

⋮

101  101  VAC  6
 ;

param: stateInPosAct: ActIn :=

1  1  1  1  none  1
1  1  1  1  LLIN  2
1  1  1  1  ACT  3
1  1  1  1  IPT  4
1  1  1  1  IRS  5
1  1  1  1  VAC  0
1  1  27  1  none  0
1  1  27  1  LLIN  0
1  1  27  1  ACT  0
1  1  27  1  IPT  0
1  1  27  1  IRS  0
1  1  27  1  VAC  6
2  1  1  1  none  1

⋮

101  101  100  15  VAC  6
 ;
```

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