Extinction probabilities for tsetse (*Glossina* spp.) in a world of changing climate

by

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Date: 2020/07/25 .....

Abstract

Extinction probabilities for tsetse (*Glossina* spp.) in a world of changing climate

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Dissertation: PhD (Maths)

December 2020

Tsetse (*Glossina* spp) transmit trypanosomiases, as sleeping sickness to humans and nagana to livestock. These continue to have negative impacts on health and wealth in the African continent. In recent years, treatment, and vector control, have helped to reduced disease burden and the World Health Organization set 2020 as a target year for eliminating the disease in humans. Tsetse populations have also declined in parts of Africa due to climate change and human encroachment. In the fight against trypanosomiases, there is a continuing need to improve understanding of tsetse population dynamics – and particularly the conditions under which tsetse populations persist, and the implications for tsetse control/eradication in a changing world. We explore here five primary objectives. Firstly, we revisit a branching process model developed for tsetse population growth and estimates for extinction probabilities. We improve the model by modifying it to work for more realistic situations where, for example, male to female sex ratios in the population are not necessarily one-to-one. We estimate extinction probabilities as a function of the probability that a deposited larva is female, and show that tsetse populations will thrive better when there are slightly more females than males in the population. We confirm that daily mortality rates $\geq 3.5\%$ ensure eradication of closed populations of tsetse. Secondly, we simplify the mathematical derivation of earlier estimate for extinction probabilities and carry out global uncertainty and sensitivity analyses on extinction probabilities, using Latin Hypercube Sampling and Partial Rank Correlation Coefficient methods. We show that adult female mortality has the highest correlation with extinction probability. We caution

that a new tsetse control method, which proposes a strategy combining Sterile Insect Techniques (SIT) with increased pupal mortality, may not offer any added benefit for tsetse eradication. Thirdly, we estimate extinction probabilities, times to extinction and growth rates as a function of temperature for tsetse populations. We provide temperature bounds for tsetse persistence, and suggest that future control efforts should consider the impact of changing climate on the distribution and abundance of tsetse populations. Fourthly, we develop a general model for tsetse population persistence, and show that previous models are special cases of our current model. While extinction probabilities are sensitive to changes in the point of the life cycle at which we count the population, the reproduction number is independent of the counting point chosen. Finally, we derive the intrinsic rate of increase for tsetse populations using the Euler-Lotka equation. We use temperature data, and tsetse population estimates from a mark–recapture exercise, to test our model's validity, and show that our results are comparable to estimates derived from the data. We estimate the intrinsic rate of increase for tsetse populations in the neighbourhood of Rekomitjie Research Station in Zimbabwe, using as input average daily temperatures from 1960–2018. We created multiple climate change scenarios, using 2018 daily temperatures as a baseline. We predict that a warming rate of 0.08°C per-year could drive tsetse populations to extinction in the neighbourhood of Rekomitjie within the next 50 years.

Uittreksel

Uitwissing waarskynlikhede vir tsetse (*Glossina* spp.) In 'n wéreld van veranderende klimaat

("Extinction probabilities for tsetse (Glossina spp.) in a world of changing climate")

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Proefskrif: PhD (Maths)

Desember 2020

Tsetse-vlieë (*Glossina* spp) dra trypanosomiasis oor, bekend as slaapsiekte by mense en nagana by vee. Dit het steeds 'n negatiewe invloed op die gesondheid en welvaart op die vasteland van Afrika. In onlangse jare het die behandeling en vektor kontrole gehelp om die las van siektes te verminder, en WGO het 2020 as 'n teikenjaar vir die uitwissing van die siekte by mense gestel. Tsetse-bevolkings het ook in dele van Afrika ernstig afgeneem as gevolg van klimaatsverandering en menslike nedersettings wat habitat oorneem. In die stryd teen trypanosomiasis is daar 'n voortdurende behoefte om die begrip van die tsetse-bevolkingsdinamika te verbeter - veral die omstandighede waaronder tsetse-bevolkings voortbestaan, en die gevolge vir die beheer van die tsetse-bevolking in 'n veranderende wêreld. Hier word vyf primêre doelstellings ondersoek. Eerstens kyk ons na 'n vertakkingsprosesmodel wat ontwikkel is vir die groei van die bevolking en die beraming van waarskynlikhede vir uitsterwing. Ons verbeter die model deur dit aan te pas vir meer realistiese situasies waar byvoorbeeld manlike-tot-vroulike geslagsverhoudings in die bevolking nie noodwendig een-tot-een is nie. Ons skat die waarskynlikheid van uitsterwing as 'n funksie van die waarskynlikheid dat 'n afgesette larwe vroulik is, en toon dat die tsetse-bevolkings beter sal floreer as daar 'n bietjie meer vroulike as manlike vlieë in die bevolking is. Ons bevestig dat daaglikse sterftesyfers van $\geq 3.5\%$ die uitsterwing van geslote tsetse-bevolkings verseker. Tweedens vereenvoudig ons die wiskundige afleiding van vroeëre beramings vir die uit-

sterwing waarskynlikhede en voer ons globale onsekerheid en sensitiwiteitsanalises uit oor die uitsterwing waarskynlikhede, met behulp van Latynse Hypercube steekproefneming en gedeeltelike rang korrelasie koëffisiënt metodes. Ons toon aan dat sterftes van volwasse vroulike vlieë sterk gekorreleerd is met die waarskynlikheid van uitsterwing. Ons waarsku dat 'n nuwe metode, waarin 'n strategie voorgestel word waarin Steriele Insekstegnieke (SIT) gekombineer word met verhoogde vrektes in die papies, geen ekstra voordeel vir die uitroei van tsetse kan bied nie. Derdens skat ons die waarskynlikheid van uitsterwing, tye tot uitsterwing en groeitempo as 'n funksie van temperatuur vir tsetse-bevolkings. Ons bied temperatuurgrense vir tsetse-volharding, en stel voor dat toekomstige beheerpogings die impak van veranderende klimaat op die verspreiding en oorvloed van tsetse-bevolkings moet oorweeg. Vierdens ontwikkel ons 'n algemene model vir volharding van die tsetse-bevolking en toon dat vorige modelle spesiale gevalle van ons huidige model is. Terwyl die waarskynlikheid van uitsterwing gevoelig is vir veranderinge in die punt van die lewensiklus waarop ons die bevolking tel, is die reproduksiegetal onafhanklik van die gekose telpunt. Laastens verkry ons die intrinsieke toename in tsetse bevolkings met behulp van die Euler-Lotka vergelyking. Ons gebruik temperatuurdata en bevolkingsberamings verkry deur 'n "mark-recapture" eksperiment, om die geldigheid van ons model te toets en om aan te toon dat ons resultate vergelykbaar is met die beramings wat uit die data verkry is. Ons skat die intrinsieke groeitempo van tsetse-bevolkings in die omgewing van die Rekomitjie-navorsingsstasie in Zimbabwe, en gebruik die gemiddelde daaglikse temperatuur tussen 1960 en 2018 as 'n veranderlike. Ons het verskeie klimaatverandering scenario's geskep met die daaglikse temperatuur van 2018 as 'n basislyn. Ons voorspel dat 'n opwarmingstempo van 0.08°C per jaar kan lei tot uitsterwing van tsetse-vlieg bevolkings binne die volgende 50 jaar in die omgewing van Rekomitjie.

Acknowledgements

No amount of words could ever describe the depth of my gratitude to my supervisor, Professor John Hargrove, who invested enormous time and energy in ensuring that I have the right exposure and training during my PhD journey. You have showed me, among other things, how to be firm and yet kind, uncompromising and yet compassionate, thorough and yet gentle. I cannot wish for a better mentor or supervisor. Thank you, I am eternally grateful. I would also like to express my deepest appreciation to Professor Jonathan Dushoff, who gave very helpful suggestions and insights which greatly improved my work.

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To the love of my life, my dear wife and best friend, Mary, who never held back her full support. How could I have managed without you? Thank you for being such a wonderful companion to me, and a caring mother to our daughter, Sonia. To my charming little angel, Sonia, thank you for gracing my life with your presence, strong character and charisma, even at your tender age. My appreciation and thanks go to my parents and siblings together with their families, your encouragement and love kept me going.

My stay at SACEMA, during my PhD, was not only enjoyable but also rewarding. All thanks to all SACEMA staff, postdocs and students. Thank you for your support and encouragement. Finally, I am indebted to my colleagues, friends, well-wishers, and former mentors who have contributed in so many ways to my academic successes.

Dedications

To Mary (my loving wife), Sonia (my beloved daughter), my parents (Samuel and Sarah Are) and my heavenly Father - Jehovah

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Chapter 1

Introduction

Tsetse (*Glossina* spp.) are biting flies of both public health and economic importance in most countries in Sub-Saharan Africa (World Health Organization (WHO), 2020). They feed exclusively on the blood of vertebrates - including game animals and livestock, but also humans, and are thereby responsible for the cyclical transmission of African trypanosomiases, tropical diseases called sleeping sickness in humans and *nagana* in livestock. In recent years populations of tsetse have declined in some parts of Africa. Studies have attributed this decline to human population growth and expansion (Reid *et al.*, 2000) as well as, in one area in Zimbabwe, to increased temperatures (Lord *et al.*, 2018). Various stages of the tsetse life cycle depend on different climatic variables such as rainfall and humidity, but the flies are most sensitive to changes in temperature. Therefore, as average temperatures continue to increase and impact tsetse populations in Africa, it is important to continue to improve knowledge about tsetse population dynamics, tsetse control methods and their effectiveness, and the impact of changing temperature scenarios on the probability of extinction for tsetse populations in the continent.

1.1 The life cycle of the tsetse is temperature dependent

The life cycle of the tsetse involves four distinct stages, namely, egg, larva, pupa, and adult. Figure 1.1 shows the simple life cycle of the tsetse and different duration of each stage, which are all temperature dependent. The female tsetse generally mates only once in her lifetime, storing the sperm in spermathecae and using small amounts to fertilize her eggs one at a time. The fertilized egg develops into a larva, which is retained within the fly's uterus and nourished with a "milk", rich in fat and protein, provided via a modified vitelline gland (Leak, 1999). The larva reaches full develop-

ment 8-10 days after ovulation and is then deposited, generally in shaded conditions on soft soil. The larva does not feed after it is deposited: instead it buries itself a few cm below the surface and pupates almost immediately. The adult fly emerges after a pupal period that depends on temperature: 20 days at 30°C and 47 days at 20°C (Hargrove, 2004).

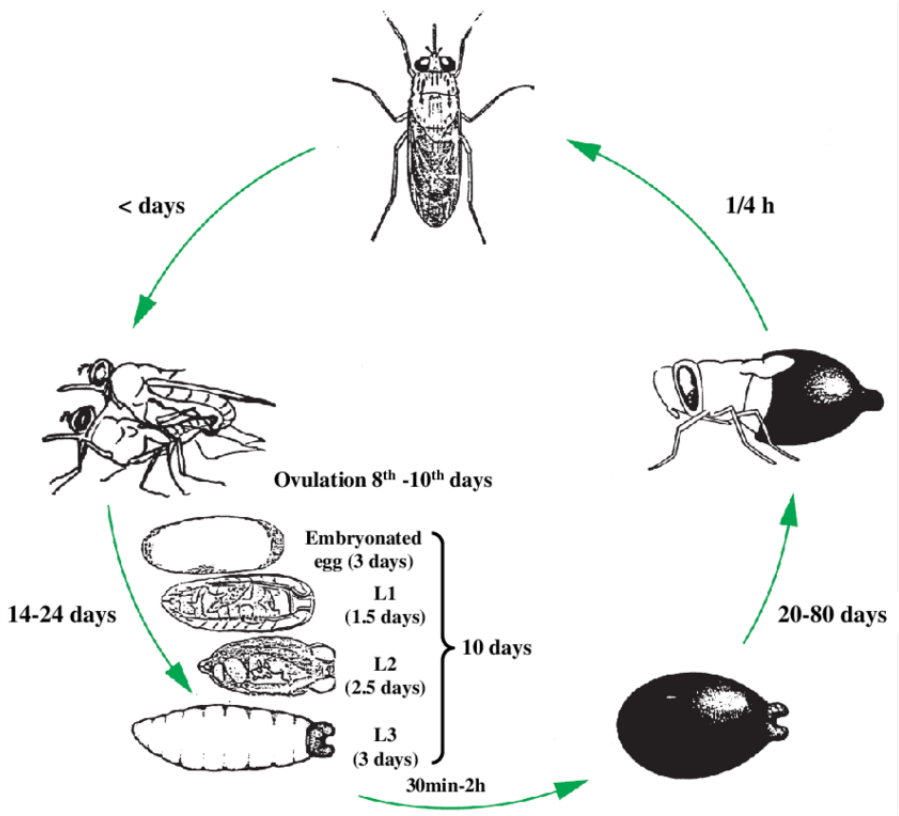

Figure 1.1: The life cycle of the tsetse. Different life stages of the tsetse (Larva, Pupa, Newly emerged adult, and Mature adult). The rate of development at the different life stages is temperature dependent. This Figure is reproduced from Cuissance (1989)

Temperatures play a key role at every stage of the tsetse life cycle. The time taken before the first larva is produced by a female is always longer than the time interval between subsequent larvae: this is because the first 2-3 blood meals need to be used to develop the flight musculature of the newly emerged female and to build up her fat levels. Accordingly, the first larva is generally only produced about 16 days after the emergence of the female adult. Subsequent inter-larval periods range from 8 to 12 days depending on temperature. Mortality at different stages of the fly's life cycle varies under different climatic conditions. Pupal mortality increases with extremes of temperature, both hot and cold. Mortality in adult flies increases at high temperature, and this may be partly due to the increased risk involved in the need to feed more

frequently, because energy is expended more rapidly at higher temperatures (Hargrove, 2004). Temperature affects other insect vectors (e.g. mosquitoes) in similar ways to tsetse, but tsetse is unusual in its viviparity and obligate blood feeding, as well as its very low birth rates.

1.2 Tsetse and trypanosomiasis distribution in Africa

Tsetse and trypanosomiases have affected not only the health and well-being of people living in Sub-Saharan Africa, they have also, for centuries, been partly responsible for the limited economic growth in some parts of the region. Even now they continue to limit livestock farming in tsetse- and trypanosomiases-endemic regions (Steverding, 2008).

Trypanosomiasis distribution in Africa coincides with the distribution of the disease vector - tsetse. Depending on classification, there are 29 - 31 species and subspecies of tsetse. Only six of these taxa have been found to be capable of transmitting the two pathogenic human parasites - *Trypanosoma brucei gambiense* and *T. b. rhodesiense* (World Health Organization (WHO), 2020). While *T. b. gambiense* causes chronic human sleeping sickness found in West and Central Africa, *T. b. rhodesianse* is responsible for the acute form of the disease found in Eastern and Southern African sub-regions. The two human forms of the disease have different epidemiological characteristics (Franco *et al.*, 2014). *T.b. gambiense* is responsible for 98% of all sleeping sickness cases. The Democratic Republic of Congo accounts for 70% of all reported human sleeping sickness cases in the last 10 years (World Health Organization (WHO), 2020). Some species of tsetse that have been confirmed, in the field, as vectors for human sleeping sickness are:

- *G. fuscipes* - Riverine tsetse species that are mostly found in areas with high humidity, rain forests and forests that are close to rivers and lake shores. They occur in Cameroon, Democratic Republic of Congo, Gabon, and the southern part of Chad. They are vectors for both *T.b. gambiense* and *T. b. rhodesianse* (Franco *et al.*, 2014).
- *G. palpalis* - Found in West and Central Africa. Their natural habitat is dense vegetation close to rivers or other water sources. These species transmit *T. b. gambiense*.

- *G. morsitans* - These species are found in savannah woodland or open woodland habitats. They occur in East and Southern Africa. They are responsible for transmitting *T. b. rhodesianse*.

Glossina vectors responsible for transmitting various trypanosome agents which cause nagana in varieties of livestock in Africa, include: *G. swynnertoni*, *G. tachinoides*, *G. longipalpis*. *G. tachinoides* *G. brevipalpis*, etc.

1.3 Tsetse and trypanosomiases in a world of changing climate

Over the past century, global mean temperature has increased by 0.7°C. Projections indicate that the trend will continue and that global mean temperature is expected to rise by between 1.1°C and 6.4°C by the end of this century (Intergovernmental Panel on Climate Change (IPCC), 2007). Being cold-blooded animals, tsetse body temperature is dependent on the prevailing temperature in their environment. Consequently, their metabolic rates, development and mortality rates depend on temperature and other climatic variables, such as rainfall, humidity, etc. (Hargrove, 2004). As global temperature continues to rise in different parts of the world, including Africa, the distribution of tsetse population may be altered. If this happens, it will have serious implications on the distribution and spread of trypanosomiasis (Moore *et al.*, 2012).

Trypanosomiasis has been identified as one of vector-borne diseases that climate change is expected to affect. A likely, perhaps short-term, effect will be an increase in the incidence of the disease as more people become exposed to tsetse in places that were initially too cold but may become optimal for tsetse population as those places become warm enough due to climate change (Lord *et al.*, 2018). Climate warming may lead to shifts in tsetse distribution in Africa. Some places are already becoming too hot for the flies, whereas, other formerly cool regions are now warming up. In the next 50 to 100 years, there is a high chance that the geographical region that is suitable for *T. b. rhodesianse* transmission may change in East and Southern Africa (Moore *et al.*, 2012).

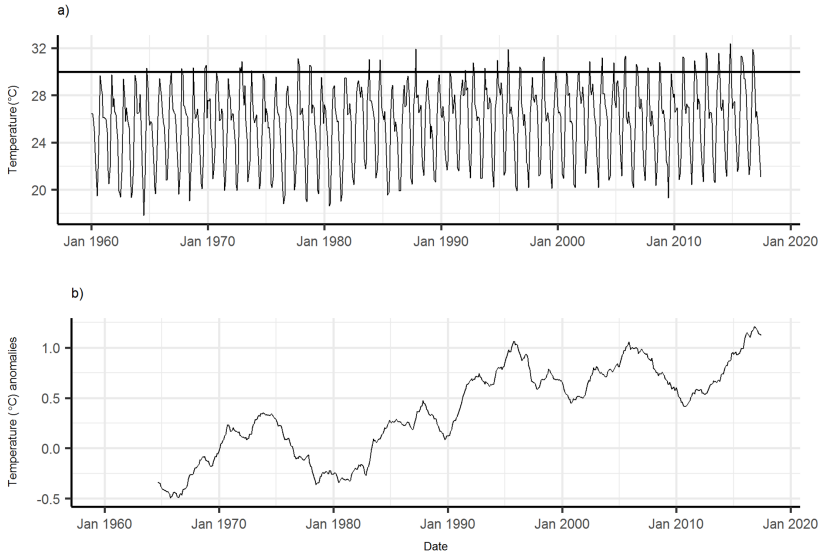

Figure 1.2: Temperature in the Zambezi Valley of Zimbawe: (a) The solid line through 30°C allows the reader to see the number of times, between 1960 and 2018, that average monthly temperatures have exceeded 30°C. (b) Temperature anomaly relative to 1960 - 1990 baseline, calculated from five year running means of average monthly temparture. Reproduced from Lord *et al.* (2018)

The Zambezi Valley of Zimbabwe provides a good example of the effect of changing temperature on the dynamics of local tsetse populations. At Rekomitjie Research Station, monthly average temperature has increased by 2°C during the hot dry season over the past 27 years. Extreme temperature events also occur with increased frequency and intensity (Fig. 1.2). These high temperatures have been associated with a sharp decline in tsetse populations in the Zambezi Valley over the last two decades (Lord *et al.*, 2018)(Fig. 1.3).

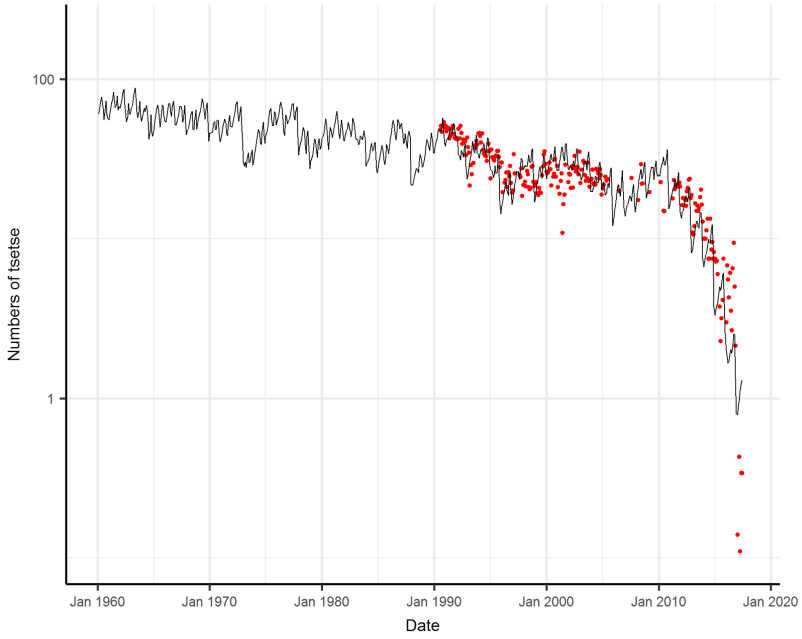

Figure 1.3: Tsetse populations in the Zambezi Valley of Zimbawe. The red dots are tsetse catches Reproduced from Lord *et al.* (2018).

If the observed decline in tsetse populations in the Zambezi Valley is true for other parts of Zimbabwe, tsetse population may witness local extinction in the hotter areas of Zimbabwe, while the cooler region may witness emergence of tsetse (Lord *et al.*, 2018).

1.4 Motivation and Statement of the problem

Tsetse have very low birth rates: at 25 °C they produce only a single larva at approximately 9-day intervals. The larva pupates almost immediately, and the pupa takes another 30 days to emerge as an adult fly. These intervals decrease with increasing temperature but, regardless of temperature, it is obvious that the reproductive rate is very slow in tsetse compared with almost all other insects. It follows, therefore, that it will be possible to control or even to eradicate tsetse populations using any technique which causes a modest, sustained increase in adult female mortality. Eradication of tsetse is thus, in principle at least, a simple and effective way of removing transmission of infection.

Additionally, during the hot-dry seasons in the Zambezi Valley, for instance, high temperatures usually account for massive losses in both the pupal and newly emerged

adult tsetse (Ackley and Hargrove, 2017). In principle, therefore, if temperature induced mortality is high enough and sustained over an extended period, such that the death rate outweighs the birth rate consistently, the population will eventually go extinct.

The research question for this work involves investigating whether increasingly high temperatures recorded in the Zambezi Valley, due to climate change, will be capable of driving tsetse populations to extinction at Rekomitjie in the near future.

A previous study used stochastic branching process to estimate extinction probabilities and time to extinction for tsetse populations, where temperature and other climatic variables are assumed to be time invariant (Hargrove, 2005). This assumption is not realistic because all of the vital rates involved in the tsetse life cycle, are temperature dependent. Moreover, temperatures vary cyclically, both diurnally and seasonally, with significant impact on tsetse mortality and natality rates.

This study will offer a realistic view of how the extinction probability for tsetse populations is related to climate, particularly temperature. This study will, potentially, inform policy on tsetse control techniques when climatic conditions are varying with time. It is our hope that the methodology developed in this study will be transferable to the study and understanding of other insect-borne diseases, like malaria, chikungunya fever, Chagas disease etc., whose spread and distributions are also temperature dependent. The mathematical framework is, to an extent, applicable in the study of the population dynamics of other insect populations subject to varying environments due to global climate change.

1.5 Study aim and objectives

1.5.1 Aim

The overall aim of this study is to estimate extinction probabilities for tsetse populations in field situations, where temperature and other climatic variables are changing both diurnally and seasonally. We also aim to predict when global climate change will lead to tsetse populations extinction in some parts of Africa.

1.5.2 Objectives

The objectives of the research project are;

- Re-visit and improve previous estimates for extinction probabilities for populations of tsetse.
- Carry out global uncertainty and sensitivity analyses to determine important parameters for the extinction probability and assess their implication for tsetse control efforts.
- Estimate the extinction probabilities for tsetse at fixed temperatures in different climatic settings.
- Determine the intrinsic rate of natural increase for tsetse populations, in situations where temperature varies cyclically within the life cycle of tsetse.
- Predict tsetse population dynamics and extinction probabilities as functions of projected temperatures for Rekomitjie, Zimbabwe.

1.6 How this work is organized

This thesis is by publication. Chapter 1 presents a general introduction, motivation, statement of the problem, and the aim and objectives of the thesis. Chapter 2 is comprised of the literature review. Each chapter from chapter 3 to chapter 7 presents a publication (either published or under review). Chapter 8 highlights the key findings and overview of the project, with conclusions and recommendations.

1.7 Publications

The following is the list of publications that are included in this thesis. At different occasions aspects of this work were presented at conferences and meetings both locally and internationally. The list of conferences and meetings I attended during this study are presented under the list of publications below.

- Kajunguri D, Are EB, Hargrove JW (2019). Improved estimates for extinction probabilities and times to extinction for populations of tsetse (*Glossina* spp.) PLoS Negl Trop Dis 13(4): https://doi.org/10.1371/journal.pntd.0006973
- Are EB, Hargrove JW (2020). Uncertainty and sensitivity analyses of extinction probabilities suggest that adult female mortality is the weakest link for populations of tsetse (*Glossina* spp.). PLoS Negl Trop Dis 14(5): e0007854. https://doi.org/10.1371/journal.pntd.0007854

- Are EB, Hargrove JW (2020) Extinction probabilities as a function of temperature for populations of tsetse (*Glossina* spp.). PLoS Negl Trop Dis 14(5): e0007769.
  https://doi.org/10.1371/journal.pntd.0007769

- Are EB, Hargrove JW, Dushoff J (2020) Insect demography: does it matter if we count babies or mummies? (Submitted, Journal of mathematical biology)

- Estimating the Intrinsic Rate of Natural Increase (IRNI) for tsetse (*Glossina* spp.) populations in a changing world (in prep).

1.7.1 Conferences and meetings attended

- Oral Presentation: "Insect demography: does it matter if we count babies or mummies?" presented at the Modelling in the context of African health conference, 14-16 October 2019, UKZN, Durban, South Africa.

- Oral Presentation: "Extinction probabilities for tsetse (*Glossina* spp.) populations in a world of changing climate" presented at the meeting on "Epidemiological consequence of reproductive senescence in long-lived vectors", from 27 - 28 of March 2019 at the Liverpool School of Tropical Medicine (LSTM), Liverpool, United Kingdom.

- Oral Presentation: "The weakest link: Exploring global uncertainty and sensitivity of extinction probability for tsetse (*Glossina* spp.)" Presented at SACEMA seminar series, 17 October 2018, SACEMA, Stellenbosch University, South Africa

Chapter 2

Literature review

2.1 Introduction

Tsetse have attracted the attention of many researchers over the past 100 years. Recently several studies have been conducted on the population dynamics of tsetse, including field-based studies, experimental studies, and more recently, modelling studies (Hargrove, 1988, 1999; Barclay and Vreysen, 2011; Childs, 2013; Sedda *et al.*, 2014; Ackley and Hargrove, 2017). The impact of changing climate on the life cycle of the flies has also been investigated (Hargrove, 2001*c*,*a*; Terblanche *et al.*, 2007, 2008; Kleynhans and Terblanche, 2011; Mutika *et al.*, 2014; Alderton *et al.*, 2018; Lord *et al.*, 2018). In this chapter we give a brief historical background on tsetse population modelling studies, and discuss some published studies in the literature on the interaction between tsetse populations and climate. Finally, we review works on the extinction probabilities for populations of tsetse focusing on stochastic branching process approaches.

2.2 Mathematical modelling of tsetse population dynamics

One of the earliest pioneering works that used analytical approaches to understand key aspects of tsetse population dynamics is the work by Rogers and Randolph (1984*c*), where attempts were made to estimate tsetse mortality based on ovarian age distribution data. They used simple exponential decay function to derive estimates for mortality rates in female *G. p. palpalis* populations at different sites in Ivory Coast. The modelling framework was used to estimate tsetse mortality from ovarian age data,

and the life-time fertility of female tsetse in the wild. They suggested a threshold value of 0.0355 for daily mortality rate in female tsetse, and concluded that any tsetse population that is experiencing daily mortalities above this threshold cannot persist, unless the population is replenished by invading flies from neighbouring patches. They assessed the impact of different climatic factors on tsetse and found that mean environmental temperatures have the strongest impact on the mortality rates. Furthermore, they obtained a closed form expression for life-time fertility of female tsetse as a function of daily mortality rate. Their modelling framework, albeit simple and relatively straightforward, drew needed attention to the usefulness of mathematical techniques in understanding key aspects of tsetse biology, especially those relating to tsetse management and control.

In an accompany paper (Rogers and Randolph, 1984*d*), the authors seek to provide evidence for density-dependent effects in tsetse populations. They estimated the rate of increase (r) from tsetse life tables, and used it as a metric to assess the impact of density-dependent effects on populations of tsetse. They found, for both male and female *G. palpalis*, a negative relationship between the per capita r and tsetse population density. The authors suggested that tsetse populations are subjected to both direct and indirect effects of the population density. For instance, pupae losses are significantly higher with increasing pupal densities, and feeding successes are also determined by population densities. They concluded that, for tsetse control effort to have a good chance of success, density-dependent effects must be accounted for.

The above authors (Rogers and Randolph, 1984*a*) proposed a simple mathematical equation to estimate tsetse daily mortality from ovarian age data, during and after insecticide treatment. They proposed an analytical method for estimating the effectiveness of Sterile Insect Technique (SIT) on tsetse populations size at equilibrium. Their preliminary results show that the level of effectiveness of insecticide treatment is largely dependent on the population density before treatment. Furthermore, they found that the annual mean number of flies caught per trap decreases as the mean annual mortality rate increases. They derived a simple mathematical expression that relates the number of flies surviving a given level of mortality and the adult population size. They suggested a framework for tsetse control management which seeks to integrate analytical, biological and technological techniques to optimize tsetse management strategies. They concluded that SIT can only start having any effect on reducing tsetse populations when the released flies can achieve 60 to 70% sterility in the population. This work, as well as the two preceding papers mentioned above, emphasizes the importance of mathematical models in improving understanding of tsetse popu-

lation dynamics, thereby facilitating the development and implementation of control measures that will achieve the highest reduction in tsetse populations with minimal efforts.

In retrospect, some of the assumptions in the Rogers and Randolph models are too simple, and sometimes unrealistic, and these might have limited the accuracy of some of their results. For example, the impact of temperature variation during tsetse life cycle were not captured in their modelling framework. Also, most of their results are based on the assumption that tsetse populations are at equilibrium and therefore the age distribution is stable. Other researchers have discussed these matters in some of the papers we will highlight here. In spite of the obvious limitations of these pioneering works, they contributed considerably to the advancement of the use of mathematical models in the field of tsetse population dynamics.

Several of the notable early works in the application of mathematical modelling to improving understanding of important aspects of tsetse population dynamics, were done by Hargrove (1981, 1988, 1993, 1994, 2000, 2001*a*, 2005). This study deployed several mathematical tools including, but not limited to, birth – death processes, deterministic models, stochastic branching processes, age-structured transmission matrices etc., to unravel key insights into tsetse biology in general, with important implication for tsetse control practices. In the following paragraphs we will review some pioneering works that considerably advanced the field of tsetse and we present their key findings.

A first order kinetic system in form of linear Ordinary Differential Equation (ODE) was used in Hargrove (1981) to model populations of *G. m. morsitans* and *G. pallidipes* in order to provide better estimates for tsetse populations sizes from mark-recapture experiments and removal trapping experiments. The model parameters were estimated from data using nonlinear regression methods. The study reported significant discrepancies in population size estimates obtained from mark-recapture and removal trapping methods, and further studies were called for on the impact of various assumptions on the model results, such as density-dependent mortality rates in both pupae and adult stages.

A Leslie matrix approach was used to estimate tsetse population growth rate as a function of different parameters representing tsetse population vital dynamics (Hargrove, 1990). The growth rate was obtained as the spectral radius of appropriate Leslie matrices. Various combinations of values of pupal duration, period between emergence and first larviposition, adult daily mortality, and pre-adult daily survival probability,

were used to calculate the limits to tsetse population growth. Sensitivity analysis showed that growth rate is highly sensitive to daily adult mortality, whereas pupal duration has no effect on tsetse growth rate when the population is at equilibrium. It was suggested that a 3% imposed daily adult mortality will ensure local extinction of tsetse populations in most field conditions. Several studies have now corroborated these findings. In a similar work, Williams *et al.* (1990) estimated growth rates for populations of *G. pallidipes* Austen as a function of the daily mortality rate in pupae and adult tsetse. They used the Euler-Lotka equation and a simulation model to find the impact of high mortalities on the age distribution of tsetse populations. They found that high mortality rates could destabilise tsetse age distribution during hot seasons, and if no additional mortality is imposed on the population, through control efforts e.g., insecticide treatments, it will take a generation (less than 2 months at 25°C (Are and Hargrove, 2020*a*)) for tsetse population to achieve a new stable age distribution. If additional mortality were imposed, it could take up to 100 days for the age distribution to stabilise. Although the methods used in this study are simple and straightforward, the study sheds light on the significant impact of tsetse mortality on the population growth rate. Tsetse mortalities can therefore be fully exploited to achieve tsetse control and/or elimination. Jarry *et al.* (1996) also investigated the limits for tsetse population growth rate using a modified Leslie matrix method. Most of their findings are consistent with previous studies on this subject (Hargrove, 1988; Williams *et al.*, 1990). Furthermore, their sensitivity analysis suggests that tsetse population growth rates are particularly sensitive to daily survival rate for newly emerged adults, a factor that should be accounted for in tsetse control planning and implementation.

Hargrove (1990) released marked male and female *G. m. morsitans* on the day of their emergence of adults and used the patterns of serial recaptures to estimate age-specific mortality rates. The study found a strong association between age and mortality rates. The study suggests that daily mortality rates among female flies are highest immediately after adult emergence, falling sharply over the first 10 days of adult life - once the fly has taken its first blood-meals. The mortality rate is then remarkably low for up to 50 days, before aging effects begin to become evident. Insect senescence in general is largely overlooked in modelling studies, and even though similar aging/mortality may be less pronounced in, for instance, mosquito, aging effects may be an important consideration for control of many insect populations.

Hargrove (2000) used a deterministic diffusion model to predict the rate of tsetse re-invasion in areas that have initially witnessed significant reduction in tsetse numbers

due to control efforts, but where control efforts have then been suspended. Although this approach might have overestimated the speed of tsetse re-invasion, it provided evidence that shows the dangers of suspending control efforts too early, especially when there are still small pockets of tsetse spread over the cleared area, or when the cleared area is relatively small and surrounding areas are untreated.

Other noteworthy tsetse modelling work include those of Jarry *et al.* (1999) who used maximum likelihood methods to estimate tsetse survival rate as function of three age categories, and Gouteux *et al.* (2001) who used a simple density-dependent model, in the form of a first order ordinary differential equation, to estimate tsetse population size from trapping experiments. Moreover, a similar work that assumed tsetse populations are not closed, (i.e. there is in-and-out migration of tsetse in the population) was presented in Artzrouni and Gouteux (2003) and used to estimate tsetse populations from trapping data.

More recently, complex modelling tools have been built and used to understand tsetse population dynamics. Researchers have used simulation studies (Vale and Torr, 2005), some incorporating spatial complexities (Peck, 2012), others have used a wide variety of mathematical models (Fall *et al.*, 2011; Hargrove *et al.*, 2012; Lord *et al.*, 2017; Ackley and Hargrove, 2017), and also individual based models (Muller *et al.*, 2004; Lin *et al.*, 2015; Alderton *et al.*, 2018), to address key questions in tsetse biology. As computational resources become more available and accessible, modellers have continued to improve on existing models, and building new ones that have the capacity to capture different complex aspects of tsetse population dynamics, thereby improving the accuracy and usability of model predictions.

2.3 Modelling tsetse population dynamics in a changing world

One of the early modelling studies linking tsetse fly mortality to climate was done by Rogers and Randolph (1984*c*), who developed analytical techniques to analyse data collected on *G. palpalis palpalis* during almost three years of study in Ivory Coast. They estimated the resilience of local fly populations in different settings. Of all the climatic factors considered, the daily mean temperature of the previous month was found to have the greatest impact on seasonal fluctuations in overall fly mortality.

Other studies have established the fact that the population dynamics of the tsetse fly is controlled by temperature. Both birth and mortality rates are temperature

dependent (Phelps and Burrows, 1969*b*; Hargrove, 2004). For different species of tsetse, a high temperature is responsible for different levels of mortalities *in utero* (loss to abortion). It may be as high as 3% during the hottest season at Rekomitjie, Zimbabwe (Hargrove, 1999).

Several researchers have studied the impact of temperature on the life stages of the fly. For instance, in a laboratory study, Phelps and Burrows (1969*b*) found that more than 50% of the pupae die when they are exposed to temperatures ≥ 36°C, for more than 6 hours. The influence of high temperature is even more apparent in young adult flies. Moreover, Pagabeleguem *et al.* (2016) studied the influence of temperature and relative humidity on the mortality of three strains of *G.p. gambiensis* in the laboratory. They found that for all strains, the median limit of survival, at 31°C, was four days and 2 days at 35°C. The temperature survival threshold for all strains was 32°C. Very low temperatures can also be fatal for the flies (Terblanche *et al.*, 2008).

In recent times, there has been an increased interest in the impact of climate on tsetse population dynamics. Most studies have found a strong relationship between tsetse population dynamics and climate, especially temperature. And this has a profound impact on the distribution and spread of the trypanosomiases (Torr and Hargrove, 1999; Terblanche *et al.*, 2008; Moore *et al.*, 2012).

Madsen *et al.* (2013) developed a mathematical model that coupled tsetse population dynamics and the spread of HAT, to assess the impact of climate change on trypanosomiasis. They carried out a sensitivity analysis on the coupled model to determine which parameters are important for the spread of the disease. They found that the model was most sensitive to tsetse related parameters that are temperature dependent. Although the study is more of a theoretical exercise, it however gave evidence that tsetse populations are highly dependent on temperature, and that tsetse control is an important tool for ensuring disease control. They concluded that climate change will impact not only the future distribution of tsetse but also the future spread of trypanosomiasis.

Several experimental studies have been conducted on the interaction of a variety of metabolic processes of various species of the tsetse and climatic factors such as temperature and relative humidity (Terblanche *et al.*, 2007; Kleynhans and Terblanche, 2011). Global climate change over recent decades has involved changes in temperature and humidity, and the long-term impact of these on tsetse population dynamics is yet to be fully seen. There is a clear consensus in both modelling and experimental studies, as

well as field studies, that temperature is a major driver of tsetse population dynamics. Consequently, as average temperatures continue to increase due to climate change, future distribution of tsetse and, by implication, the future spread of trypanosomiasis is a major cause for concern.

A recent study (Lord *et al.*, 2018) developed a deterministic model for tsetse populations, and allowed input parameters, such as pupal mortality, adult mortality and inter-larval period to be temperature dependent. Using the mathematical relation between input parameters and temperature, the model was fitted to the tsetse catch data obtained from Rekomitjie Research Station, in the Rekomitjie neighbourhood. The model shows that increases in temperatures may explain the decline in populations of tsetse in the Zambezi Valley of Zimbabwe, where temperatures have increased in the past 27 years. Mean daily temperature has increased by 0.9°C when measured over the whole year, and by 2°C in the hottest periods of the year. This evidence raises the possibility that these increasing temperatures could lead to local extinction of tsetse populations. Although the model produced a good fit to the data, and provided strong evidence that climate change has indeed impacted tsetse populations severely at Rekomitjie, it failed to provide any clear insights regarding tsetse extinction probabilities and times to extinction.

2.4 Application of branching processes in tsetse population studies

When populations are large enough and unperturbed, deterministic models are suitable for modelling the dynamics of such populations. But this approach is not appropriate when population sizes are small, especially when attempts are made towards control and eradication (Hargrove, 2004). A more suitable approach, in this case, is the stochastic model, capable of predicting trends in small populations under perturbation, as in the case of tsetse fly populations, perturbed by temperature and other climatic factors.

The stochastic branching process has an interesting history. In the mid-19th century, aristocratic families in Victorian England were concerned about the possibility of their family names going extinct. Sir Francis Galton thus posed a question:

"*How many male children (on average) must each generation of a family have in order for the family name to continue in perpetuity*?"

This was solved by his friend Rev. Henry Watson. A similar problem was developed and analysed independently, by Iréné-Jules Bienaymé, in 1845. Following these studies, branching processes have found application across fields of many human endeavour - biology, nuclear physics, demography etc.

Branching process can be defined easily as a system of reproducing particles (individuals, cells, tsetse), which live for a random time period, and produce a random number of offspring and die. The offspring are assumed to reproduce independently with identical probability distribution (Axelrod and Kimmel, 2015).

The theory of branching processes is well developed mathematically, and has been used extensively to understand disparate fields of science. It has been applied to problems in evolutionary theory, molecular biology, cell kinetics, applied population biology (Jagers, 1995) and, more recently, epidemiological modelling (Jacob, 2010).

Hargrove (2005) appears to be the first researcher to use a stochastic branching process to estimate the probability of extinction for populations of tsetse flies. He derived equations for the probability of extinction, the mean and variance of the population size, and the time to extinction of tsetse populations. The study assessed the impact of various control measures on the probabilities and times to extinction for populations of tsetse, and found that a sustained daily mortality of about 3.5% among adult female tsetse will be sufficient to ensure extinction of any tsetse population. Moreover, extinction can be achieved without additional mortality if females mate with a sterile male on greater or equal to 90% of occasions. The study provided a good framework for assessing the effectiveness of various control measures for tsetse populations. The study suggested that control measures that can achieve high mortality rates in adult flies, should be used whenever possible to achieve tsetse eradication. Other techniques, such as SIT, targeting reduction in tsetse reproduction rates, should be used only when cheap methods have failed to achieve tsetse eradication.

2.5 Research gap

Hargrove (2005) made the restrictive assumption that male and female offspring are produced with equal probability, and most of the proofs are omitted in the original paper. Furthermore, the model was derived under a given set of conditions assumed to be constant in time, thereby failing to associate the input parameters to varying climatic conditions. These assumptions made the model simple and tractable. In practice, however, the life cycle of the tsetse fly depends on weather conditions that

are constantly changing. Pupal duration, pupal mortality and adult mortality all depend on temperature. For instance, field studies show that the pupa develops to an adult within 20 days at 30°C and 47 days at 20°C (Hargrove, 2004). We will develop a more realistic model which allows temperature and other climate variables to vary with time. Furthermore, a closed form expression for extinction probabilities for tsetse population provided a unique opportunity to perform a detailed uncertainty and sensitivity analysis on the extinction probability, to identify key parameters that will inform appropriate control methods to achieve tsetse population extinction. This was not explored in the original study. Finally, the modelling framework was based on counting only newly emerged adult female tsetse in the population: it failed to account for the possibility of counting tsetse at different life stages. This thesis aims to bridge these gaps.

2.6 Conclusion

We have reviewed the body of work that essentially makes up a brief history of tsetse models. We have identified that considerable effort has gone into utilising mathematical tools and techniques in order to gain improved understanding of tsetse population dynamics in general. We have also discussed some important studies that used mathematical models to assess the impact of changing climate on tsetse population dynamics. Moreover, we have reviewed works on the application of branching processes in tsetse population modelling, while identifying some major research gaps that we aim to fill in this study.

Chapter 3

Improved estimates for extinction probabilities and times to extinction for populations of tsetse (*Glossina* spp.)

3.1 Abstract

A published study used a stochastic branching process to derive equations for the mean and variance of the probability of, and time to, extinction in population of tsetse flies (*Glossina* spp) as a function of adult and pupal mortality, and the probabilities that a female is inseminated by a fertile male. The original derivation was partially heuristic and provided no proofs for inductive results. We provide these proofs, together with a more compact way of reaching the same results. We also show that, while the published equations hold good for the case where tsetse produce male and female offspring in equal proportion, a different solution is required for the more general case where the probability (β) that an offspring is female lies anywhere in the interval $(0, 1)$. We confirm previous results obtained for the special case where $\beta = 0.5$ and show that extinction probability is at a minimum for $\beta > 0.5$ by an amount that increases with increasing adult female mortality. Sensitivity analysis showed that the extinction probability was affected most by changes in adult female mortality, followed by the rate of production of pupae. Because females only produce a single offspring approximately every 10 days, imposing a death rate of greater than about 3.5% per day will ensure the eradication of any tsetse population. These mortality levels can be achieved for some species using insecticide-treated targets or cattle - providing thereby a simple, effective and cost-effective method of controlling and locally eliminating, and

also human and animal trypanosomiasis. Our results are of further interest in the modern situation where increases in temperature are seeing the real possibility that tsetse will go extinct in some areas, without the need for intervention, but have an increased chance of surviving in other areas where they were previously unsustainable due to low temperatures.

3.2 Author summary

We derive equations for the mean and variance of the probability of, and time to, extinction in population of tsetse flies (*Glossina* spp), the vectors of trypanosomiases in sub-Saharan Africa. In so doing we provide the complete proofs for all results, which were not provided in a previously published study. We also generalise the derivation to allow for the probability that an offspring is female to lie anywhere in the interval $(0, 1)$. The probability of extinction was most sensitive to changes in adult female mortality. The unusual tsetse life cycle, with very low reproductive rates, means that populations can be locally eliminated as long as adult female mortality is raised to levels greater than about 3.5% per day. Simple bait methods of tsetse control, such as insecticide-treated targets and cattle, can therefore provide simple, affordable and effective means of locally eliminating tsetse populations. The results are of further interest in the modern situation where increases in temperature are seeing the real possibility that tsetse will go extinct in some areas, but have an increased chance of surviving in others where they were previously unsustainable due to low temperatures.

3.3 Introduction

Whereas deterministic models of the growth of populations of tsetse (*Glossina* spp.) (Diptera: Glossinidae) are generally adequate for large populations (Williams, 1991; Rogers, 1990), stochastic models are more appropriate when numbers are small, particularly if the population approaches zero through natural processes and/or following attempts to locally eradicate the fly. At that point the focus changes from attempting to obtain deterministic predictions of future population levels, to predicting the probability that the population will go extinct, and the expected time required in order to achieve this end. Hargrove developed a stochastic model for the life history of tsetse and thereby provided estimates of the probability of extinction, and expected time to extinction, for these insects (Hargrove, 2005). Such estimates were always of interest in situations where there was pressure in favour of area-wide eradication of entire tsetse species (Vreysen *et al.*, 2013). The model provided estimates of the level, and duration, of control effort required to achieve eradication of a target population

and could thus be valuable for financial planning of tsetse and trypanosomiasis control efforts. The formulae developed were shown to provide good estimates of the time to extinction in successful operations that had already been carried out.

With the significant increases in temperature that have occurred over recent decades the model has assumed increased interest. It is becoming apparent that parts of Africa are becoming so hot that tsetse may no longer survive there. A well-documented example is the population of *G. pallidipes* Austen in parts of Zimbabwe. Whereas this species occurred in huge numbers in the area, for example, in the neighborhood of Rekomitjie Research Station, in the Zambezi Valley, the population has shrunk by more than 99.99% over the past 30 years and now appears to be on the brink of disappearing (Vale and Hargrove, 2015; Lord *et al.*, 2018). At the same time, other parts of Zimbabwe, where tsetse are not currently found - in part because winter temperatures are too low - may soon be warm enough to support tsetse. Hwange National Park, for example, supported tsetse populations prior to the rinderpest epizootic of 1896: the fly never re-established itself in the area in the 20th Century, despite the presence of an abundance of wild hosts. In part this is considered to be due to the area always having been marginal climatically: increasing temperatures may change this balance in favour of the fly.

The above considerations prompted us to revisit the original derivations, from which several things became apparent: (i) It was assumed in the original derivation that equal proportions of male and female offspring were produced by female tsetse. The equations presented were correct for this particular case - but require modification for the more general case where the probability (β) that an offspring is female lies anywhere in the interval (0,1) (Leak, 1999). (ii) At a number of points in the development it is claimed that results can be shown by induction, but the proofs are not provided. (iii) An heuristic explanation for one of the equations is misleading because it refers to a number > 1 as a probability. (iv) Finally, the development is restrictive in that it only treats the case where birth and death rates are constant over time. In the current paper we correct the first three problems and suggest ways of overcoming the fourth.

3.3.1 Basic life cycle of Tsetse

Both sexes of tsetse feed only on blood and are vectors of human and animal trypanosomiases in Africa. They are also very unusual biologically. During each reproductive event, the mature adult female tsetse ovulates a single egg that is retained in the uterus until it hatches. The resulting larva develops through three instars, nourished via a milk gland, resulting ultimately in a third instar larva that may weigh as much as,

or even slightly more than, its mother. This reproductive mechanism is termed adenotrophic viviparity. The mature late-third-instar larva is typically deposited on soft soil, into which it burrows rapidly, pupating immediately and remaining underground, without feeding further, until it develops into a young adult fly (Leak, 1999).

Given the large amount of energy and raw material required to produce the large pupa, the female only produces one pupa every $7-12$ days: and the resulting pupa takes $3-7$ weeks to develop into an adult fly - the rates for these processes depending on temperature (Hargrove, 2004). The teneral (i.e. unfed) adult emerging from the puparial case has the full linear dimensions of the mature adult, but has a poorly developed flight musculature, and lower levels of fat reserves than mature adults. The first 2-3 blood-meals must be used to build flight muscle and fat levels before the female can start producing her own pupae. Given the implicitly low birth rate, it is clear that tsetse populations can only survive if they are able to keep their mortality at low levels. In the laboratory, male and female *G. m. morsitans* can survive for up to 241 and 208 days, respectively (Chigusa *et al.*, 1997). In the field, the flies are seldom that long-lived and females survive for longer than males, sometimes surviving at least 130 days (Hargrove, 1990). There is a marked loss, with increasing age, in female reproductive potential in laboratory populations, but there is little suggestion of such an effect in field flies (Hargrove, 1999). Similarly, whereas trypanosome infection can result in increased mortality in tsetse > 50 days old, the evidence for such an effect in field flies is not as convincing. For present modelling purposes we have, accordingly, ignored any effect of trypanosome infection on tsetse survival.

3.4 Materials and methods

In this paper, we provide full details of the derivation of the formulae used and also provide a general form of the governing equation in Hargrove (2005), which can accommodate all possible values of β.

3.4.1 Model Assumptions and Development

A female tsetse generally mates only once; it is thus crucial to include in our model the probability that a female tsetse is inseminated by a fertile male. We will also assume that the probability that a deposited pupa is male or female can be anywhere in the open interval $(0, 1)$. Note that, at both endpoints, extinction occurs with probability 1, because the population will consist only of one sex of fly.

3.4.2 Parameters and Interpretations

λ	daily survival probability for adult female tsetse
ψ	daily mortality rate for adult females = -$ln(\lambda)$
φ	daily survival probability for female pupae
χ	daily mortality rate for female pupae = -$ln(\varphi)$
ν	time from adult female emergence to first ovulation (days)
ϵ	probability female is inseminated by a fertile male
τ	inter-larval period (days)
P	pupal duration (days)
$p_{n,k}$	probability female tsetse dies between pregnancy n and $(n+1)$ and produces k surviving female offspring
β	probability deposited pupa is female

The probability $p_{1,1}$ that a female survives one pregnancy and produces one surviving female offspring is calculated as follows: First, we know that a female tsetse fly is inseminated by a fertile male with a probability ϵ, then survives with probability $\lambda^{(\nu+\tau)}$ up to the time she produces her first pupa, which itself has a probability β of being female. This pupa survives the pupal period with a probability φ^P, and the mother finally dies with a probability $(1-\lambda^\tau)$ during the next pregnancy. Thus, combining all these factors, we obtain the probability that a female tsetse fly produces one surviving daughter after surviving one pregnancy as

$$p_{1,1} = \epsilon\lambda^{(\nu+\tau)}\beta\varphi^P(1-\lambda^\tau). \tag{3.1}$$

In general, the probability that a female tsetse produces k surviving daughters, after surviving n pregnancies, is given by

$$p_{n,k} = \epsilon\lambda^{(\nu+n\tau)}(1-\lambda^\tau)\binom{n}{k}\beta^n\varphi^{kP}(\frac{1}{\beta}-\varphi^P)^{n-k}, \tag{3.2}$$

for $n > 0, 1 \leq k \leq n$, and where $\binom{n}{k}$ are the binomial coefficients.

Proof of equation (3.2):

Let A_n be the event 'a mother deposits exactly n pupae', and $B_{n,k}$ be the event 'n pupae produce exactly k female adults'. We can then define

$$\begin{aligned} M_n &= P(A_n) = \epsilon\lambda^{\nu+n\tau}(1-\lambda^\tau). \\ q_{n,k} &= P(B_{n,k}|A_n). \end{aligned}$$

It is clear that

$$p_{n,k} = P(A_n \bigcap B_{n,k}) = P(A_n).P(B_{n,k}|A_n) = M_n.q_{n,k}. \tag{3.3}$$

We note that M_n refers to the mother's survival and $q_{n,k}$ refers to the pupae survival. So we can develop our proof by concentrating on the pupal survival since the product of the two gives the result of interest.

It was actually observed that equation (3.2) can be proved without resorting to induction. Note that for each pupa there are two possibilities; either it becomes an adult female or it does not. The probability that it becomes an adult female is $\beta\varphi^P$, and the probability that it does not is then clearly $(1-\beta\varphi^P)$. Since the probabilities are the same for all pupae, and these outcomes for different pupae are independent, the probability that there are k adult females from n pupae is given by a binomial distribution as

$$\begin{aligned} q_{n,k} &= \binom{n}{k}(\beta\varphi^P)^k(1-\beta\varphi^P)^{n-k} \\ &= \binom{n}{k}\beta^k\varphi^{Pk}\beta^{n-k}(\frac{1}{\beta}-\varphi^P)^{n-k} \\ &= \binom{n}{k}\beta^n\varphi^{Pk}(\frac{1}{\beta}-\varphi^P)^{n-k}. \end{aligned}$$

Thus, from equation (3.3), we obtain the expression for $p_{n,k}$ as

$$p_{n,k} = M_n.q_{n,k}$$

$$= \epsilon\lambda^{(\nu+n\tau)}(1-\lambda^\tau)\binom{n}{k}\beta^n\varphi^{Pk}(\frac{1}{\beta}-\varphi^P)^{n-k}. \tag{3.4}$$

Note that this reduces to the governing equation in (Hargrove, 2005) when $\beta = 0.5$.

Remarks:

1. The heuristic explanation for equation (3.2) in Hargrove (2005) is misleading because it terms a number greater than 1 a probability. Nonetheless, the formula is correct for the case considered, and is also correct more generally with the adjustment of that term, as the proof shows.

2. The governing equation in Hargrove (2005) works only when β=0.5. After making the correction, it can be observed that equation (3.4) works for all values of β.

Summing equation (3.2) over n leads to the probability (p_k) that a female tsetse produces k surviving female offspring before she dies. Thus

$$p_k = \sum_{n=k}^{\infty} \epsilon\lambda^{(\nu+n\tau)}(1-\lambda^{\tau})\binom{n}{k}\beta^n\varphi^{kP}(\frac{1}{\beta}-\varphi^P))^{n-k} \tag{3.5}$$

$$= \epsilon\lambda^{\nu}(1-\lambda^{\tau})\varphi^{kP}\sum_{n=k}^{\infty}\binom{n}{k}(\lambda^{\tau}\beta)^n(\frac{1}{\beta}-\varphi^P))^{n-k}. \tag{3.6}$$

Evaluating the sum gives

$$p_k = \frac{\epsilon\lambda^{\nu+k\tau}(1-\lambda^{\tau})\beta^k\varphi^{kP}}{(1-\beta\lambda^{\tau}(\frac{1}{\beta}-\varphi^P))^{k+1}} \qquad k>0. \tag{3.7}$$

The probability that a female tsetse produces at least one surviving daughter before she dies can be obtained by summing equation (3.7) over $k>0$, to obtain

$$p_{(k>0)} = \frac{\epsilon\lambda^{\nu+\tau}\beta\varphi^P}{1-\lambda^{\tau}(1-\beta\varphi^P)}. \tag{3.8}$$

(See Kajunguri *et al.* (2019) S1 Text for detailed proofs of equations (3.7) and (3.8))

Thus, the probability that a female tsetse does not produce any surviving female offspring before she dies is given by

$$p_0 = 1-p_{(k>0)} = 1-\frac{\epsilon\lambda^{\nu+\tau}\beta\varphi^P}{1-\lambda^{\tau}(1-\beta\varphi^P)}. \tag{3.9}$$

Assuming that we start with one female tsetse in the initial generation, which produces k surviving offspring, we can write the moment generating function for the next generation as

$$\phi(\theta) = \sum_{k=0}^{\infty} p_k\theta^k = p_0 + \sum_{k=1}^{\infty} p_k\theta^k.$$

Substituting for p_0 and p_k and putting the terms not involving k outside the summation sign we get

$$\phi(\theta) = \frac{A+BC(1-\theta)}{A+B(1-\theta)}, \tag{3.10}$$

where $A=1-\lambda^{\tau}, B=\beta\lambda^{\tau}\varphi^P$ and $C=1-\epsilon\lambda^{\nu}$

The extinction probability can be found by solving the quadratic equation $\phi(\theta) = \theta$, and it is the smallest non-negative root (Lange, 2010; Lange *et al.*, 1981). Thus the extinction probability is:

$$\theta = \frac{BC + A + B - \sqrt{(BC + A + B)^2 - 4B(A + BC)}}{2B}, \tag{3.11}$$

where $B \neq 0$.

This is the probability that a female tsetse population, resulting from an initial population of one adult female fly, goes to extinction. If the initial population consists of N such flies, then, assuming the independence of the probability of extinction of each female line, the probability of extinction is θ^N.

3.4.3 Mean and variance of female tsetse population at generation n

We will use the method of moments to find the mean and variance of the expected number of offspring produced. From these variables we can then derive the mean and variance of the female tsetse population at a given generation n.

By definition, the m^{th} moment of p_k is given by

$$M_m = \sum_{k=0}^{\infty} k^m p_k.$$

When $m = 1$, we obtain the first moment as

$$M_1 = \frac{\epsilon\lambda^{\nu+\tau}\beta\varphi^P}{(1 - \lambda^\tau)}. \tag{3.12}$$

And when $m = 2$, we obtain the second moment as

$$M_2 = \frac{\epsilon\lambda^{\nu+\tau}\beta\varphi^P(1 - \lambda^\tau(1 - 2\beta\varphi^P))}{(1 - \lambda^\tau)^2}. \tag{3.13}$$

(See Kajunguri *et al.* (2019) S1 Text for the proofs of equation (3.12) and equation (3.13))

The mean, or expected number of surviving daughters of female tsetse is

$$\mu = \frac{\epsilon\lambda^{\nu+\tau}\beta\varphi^P}{(1 - \lambda^\tau)},$$

and the variance is given by

$$\sigma^2 = \frac{\epsilon\lambda^{\nu+\tau}\beta\varphi^P(1-\lambda^\tau(1-2\beta\varphi^P))}{(1-\lambda^\tau)^2} - (\frac{\epsilon\lambda^{\nu+\tau}\beta\varphi^P}{(1-\lambda^\tau)})^2,$$

where

$$M(n) = \mu^n. \tag{3.14}$$

and

$$V(n) = \begin{cases} n\sigma^2, & \mu = 1 \\ \frac{(1-\mu^n)\sigma^2\mu^{n-1}}{1-\mu}, & \mu \neq 1. \end{cases} \tag{3.15}$$

$M(n)$ and $V(n)$ are the mean and variance of the size of each generation (X_n), respectively with the assumption $X_0 = 1$. Equations (3.14) and (3.15) can be shown easily by induction.

3.4.4 Time for population of the female tsetse to become extinct

From the general framework developed by Lange (Lange, 2010; Lange *et al.*, 1981) for the probability of extinction of a branching process, we have

$$\theta_n = \sum_{k=0}^{\infty} p_k(\theta_{n-1})^k, n = 1, 2, 3, \ldots \tag{3.16}$$

where θ_n is the probability of extinction at the n^{th} generation and k is the number of offspring. Equation (3.16) can be rewritten in terms of a moment generating function as

$$\phi(\theta_{n-1}) = \sum_{k=0}^{\infty} p_k(\theta_{n-1})^k = \theta_n. \tag{3.17}$$

Thus, from (3.17), extinction probabilities can be calculated by starting with $\theta_0 = 0, \theta_1 = \phi(\theta_0), \theta_2 = \phi(\theta_1)$, and continuing iteratively through the generations to obtain

$$\theta_n = \phi(\theta_{n-1}). \tag{3.18}$$

We also derived the first moments of T, based on the general formula obtained by Feller (1968) as

$$E(T^j) = \sum_{n=0}^{\infty}[(n+1)^j - n^j](1-\theta_n), \tag{3.19}$$

where (1-θ_n) = P($T > n$) and T is the extinction time. The first two moments of T are:

$$E(T) = \sum_{n=0}^{\infty}(1 - \theta_n), \tag{3.20}$$

and

$$E(T^2) = \sum_{n=0}^{\infty}(2n + 1)(1 - \theta_n). \tag{3.21}$$

Thus, using equations (3.10) and (3.18) and taking $\theta_0 = 0$, we can calculate the values of θ_n by iteration. The first two, for example, are:

$$\theta_1 = \phi(\theta_0) = \phi(0) = \frac{A + BC}{A + B}, \tag{3.22}$$

$$\theta_2 = \phi(\theta_1) = \phi(\frac{A + BC}{A + B}) = \frac{A + BC\left(1 - \frac{A+BC}{A+B}\right)}{A + B\left(1 - \frac{A+BC}{A+B}\right)}. \tag{3.23}$$

In a situation where there are N surviving females, with $N > 1$, equations (3.20) and (3.21) can be generalised. The probability of extinction at or before generation n is θ_n. If we have N surviving females, then the probability that they all become extinct at generation n is $(\theta_n)^N$. Thus,

$$E(T) = \sum_{n=0}^{\infty}(1 - (\theta_n)^N), \tag{3.24}$$

and

$$E(T^2) = \sum_{n=0}^{\infty}(2n + 1)(1 - (\theta_n)^N). \tag{3.25}$$

To estimate the mean and variance of the time to extinction for a population of N female tsetse flies, all that needs to be done is to estimate θ_n for a population consisting of a single fly, raise each of the values to power N, and obtain the appropriate sums.

3.5 Results

3.5.1 Extinction probabilities as a function of adult and pupal female mortality rates

We produced MATLAB code to solve equation (3.11) and generate the extinction probabilities for given values of parameters A, B and C. Our results were closely similar

to those previously published (Hargrove, 2005), as illustrated in Figs S1 - S5 of the S1 Text in Kajunguri *et al.* (2019). For example, for a pupal duration (P) of 27 days, a time to first ovulation (ν) of 7 days, an inter-larval period (τ) of 9 days, a probability of $\beta = 0.5$ that a deposited pupa will be female and where all females are inseminated by a fertile male ($\epsilon = 1$), the extinction probability for a population consisting of a single inseminated female fly increased linearly with adult female mortality rate (ψ), at a rate which increased with increasing pupal mortality rate (χ) (Fig S1A in Kajunguri *et al.* (2019)).

If the pupal mortality is high enough, then the probability of extinction is high even if the adult mortality is low. For example if $\chi = 0.03$ per day, then there is a greater than 40% chance that extinction will happen, even if the adult mortality rate is only 0.01 per day. Even when there was zero pupal mortality, however, extinction was certain when adult mortality rate approached levels of 0.04 per day. When the pioneer population consisted of more than a single inseminated female, the extinction probability was of course generally lower (Fig S1B in Kajunguri *et al.* (2019)). If the pupal mortality rate was even 0.005 per day, however, all populations eventually went extinct, with probability 1, as long as adult mortality rate exceeded about 0.032 per day.

3.5.2 Extinction probabilities as a function of the probability of insemination

In situations where, for example, sterile male tsetse are released into a wild population or where a population is extremely low, females may fail to mate with a fertile male and ϵ will then fall below 1. When the starting population was a single inseminated female, and with other input parameters as defined above, the extinction probability decreased approximately linearly with increasing values of ϵ (Fig S2A in Kajunguri *et al.* (2019)). Increasing the assumed value of the adult mortality rate (ψ) simply shifted the whole graph of extinction probability towards a value of 1, without changing the rate of increase of extinction probability with ϵ.

When the pioneer population was greater than 1, the relationship with ϵ was no longer linear (Fig S2B (Kajunguri *et al.*, 2019)) and, even when the starting population was only 16 inseminated females, the extinction probability was still effectively zero when the probability of fertile insemination fell to 50%. No population could avoid extinction, however, when ϵ was less than about 10%.

3.5.3 Extinction probabilities as a function of the probability a deposited pupa is female, and the death rate of adult females

Extinction is of course certain if a population consists only of one sex, but the probability of extinction goes to 1 more rapidly as the probability (β), that a deposited pupa is female, goes to 0 (all male population) than as it goes to 1 (all female population, Fig 3.1). For adult female mortality rates very close to zero, the extinction probability goes to 1 as β goes to zero: but, for higher adult death rates the limit is reached for values of $\beta > 0$. For example, when daily survival is moderately high, $\lambda = 0.98$, extinction is already certain once the female proportion among pupae drops to 30%. The minimum extinction probability across different daily survival values always occurs for a value of $\beta > 0.5$, by an amount that increases as adult female mortality increases.

3.5.4 Expected number of generations to extinction

We derived the general equation for the expected number of generations to extinction for independent lines of N females in equation (3.24). Equations (3.22) and (3.23) give the first two iterations of the probability of extinction. MATLAB code was written to solve equation (3.24) iteratively and thus find the expected number of generations to extinction. Fig S3 in Kajunguri *et al.* (2019) shows that the expected number of generations to extinction decreases with any increase in pupal mortality.

Fig S4 (A and B) in Kajunguri *et al.* (2019) show that, in the event that eradication is attempted through the release of sterile males, in order to reduce the probability that females are inseminated by fertile males, the eradication process will be much hastened if the mortality of the wild female population is also increased.

Fig S5 in Kajunguri *et al.* (2019) gives the result of the expected number of generations to extinction against the probability of insemination. From the graph, we can see that the lower the probability of insemination by a fertile male, the smaller the number of generations to extinction.

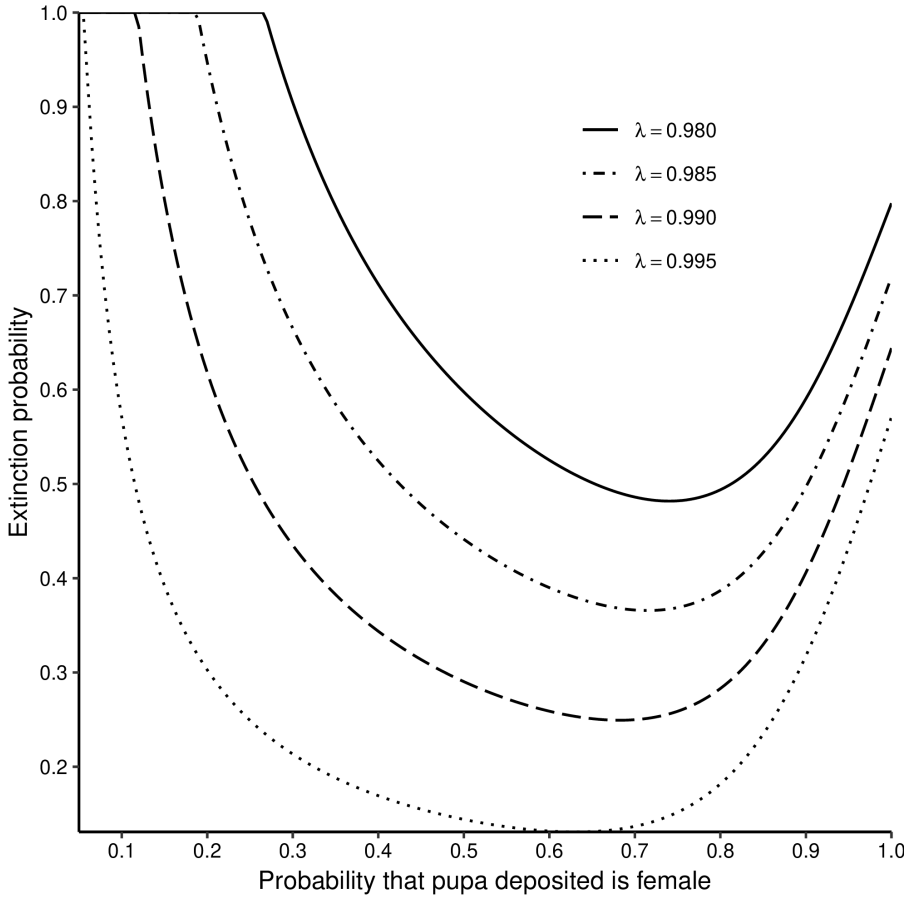

Figure 3.1: Extinction probability as a function of the probability a deposited pupa is female, and the adult survival probability.
Input assumptions: Initial population $N = 1$ inseminated female; pupal mortality rate $\chi = 0.005$ per day; probability female inseminated by a fertile male, $\epsilon = 1.0$; pupal duration, $P = 27$ days; time to first ovulation, $\nu = 7$ days; inter-larval period $\tau = 9$ days. Figures in the body of the plot show the assumed daily survival probability (λ) for adult females.

3.6 Discussion

Our results place on a firmer footing published findings based on the restrictive assumption that a deposited pupa has an equal chance of being male or female (Hargrove, 2005). Nonetheless, we confirm various findings of the earlier study. For example, it is clear that tsetse populations can exist at very low population densities, and the sensitivity analysis added in the present study, also indicates the prime importance of mortality among adult females in affecting the probability of extinction in tsetse populations. This result further supports the arguments adduced in the earlier paper regarding the efficacy, and the cost-efficacy, of "bait methods" of tsetse control – and we refer the reader to the earlier discussion (Hargrove, 2005).

For controlling the species of tsetse occurring in Zimbabwe – *G. m. morsitans* and *G. pallidipes* – the primacy of bait methods has been well established. In a mark-recapture study carried out on Antelope Island, Lake Kariba, it was estimated that 24 odour-baited insecticide-treated targets, deployed on the 5 sq km island, killed about 2% per day of female *G. m. morsitans* and 8% of *G. pallidipes* (Vale *et al.*, 1986; Hargrove and Williams, 1998). When targets were used in the Rifa Triangle, in the Zambezi Valley, at the same approximate density, populations of both species were reduced by $> 99.99\%$ and the populations in the treated area only survived through invasion from adjacent untreated areas (Vale *et al.*, 1988*b*; Hargrove, 2003*a*). Again, it was estimated that the targets were killing about 2% per day of female *G.m. morsitans* and up to 10% of *G. pallidipes*. The Rifa experiment was carried out, however, when the only odour attractants available for use with targets were acetone and 1-octen-3-ol: targets are now used with the addition of two phenols, which increase the target kill rates of *G.m. morsitans* by about 50%, and those of *G. pallidipes* by several fold (Vale *et al.*, 1988*a*; Bursell *et al.*, 1988). Moreover, the targets currently in use are nearly twice as effective as the prototypes used in the Rifa Triangle (Vale, 1993) consequently it is estimated that odour-baited insecticide-treated targets, deployed at 4 sq km in Zimbabwe will kill at least 4% per day of female *G. m. morsitans* and about 10% of female *G. pallidipes*. As is clear from Fig S1A in Kajunguri *et al.* (2019), these levels of imposed mortality are sufficient to ensure local eradication of any population of tsetse, even if the natural, adult and pupal mortality rates are zero. These theoretical predictions are borne out for *G. m. morsitans*, which was eradicated in the Umfurudzi Safari Area using targets at the above density (Hargrove, 2003*b*).

In our modelling we do not take into account the well-established age-dependent sampling biases of stationary baits such as traps and targets (Hargrove, 1991) and the estimated imposed mortality is thus an average figure. This is appropriate, however, since the additional mortality due to targets, estimated from mark-recapture data, was also a figure averaged over adult females of all ages. A suggestion of a bias that would favour targets killing larger flies finds no support in the Zimbabwe situation (Hargrove *et al.*, 2019; Mbewe *et al.*, 2018*a*).

In areas of Zimbabwe where there are cattle in tsetse areas, the use of insecticide-treated cattle provides an effective method that can be used in parallel with, or even instead of, insecticide-treated targets. The combined use of these two bait methods saw massive reductions in levels of animal trypanosomiasis in north-east Zimbabwe during the 1990s, to the point that in 1997, despite widespread monitoring of cattle, no case of animal trypanosomiasis was detected (Hargrove, 2003*b*).

In Zimbabwe, therefore, the use of any other method in addition to odour-baited insecticide-treated target, and insecticide-treated cattle, appears to constitute a waste of resources. In particular the release of large numbers of laboratory-reared sterile male tsetse appears superfluous and unjustified. In this regard the very much larger effect on the probability of extinction resulting from quite modest increases in adult female mortality stands in strong contrast to the very large reduction in female fertility that must be effected in order to achieve eradication (*cf* Figs S1B and S2A in Kajunguri *et al.* (2019)).

Since the publication of the original analysis of extinction probability for tsetse in Hargrove (2005), there has been increased interest in using insecticide-treated targets in control operations against riverine species of tsetse, such as *G. f. fuscipes* and *G. palpalis* (Lindh *et al.*, 2009; Esterhuizen *et al.*, 2011; Rayaisse *et al.*, 2011; Lindh *et al.*, 2012; Solano *et al.*, 2013; Shaw *et al.*, 2015; Tirados *et al.*, 2015; Lehane *et al.*, 2016). These species are not strongly attracted by host odour, and the kill rate per target is thus very much lower than for *G. pallidipes*: the riverine species can, however, be captured on much smaller targets [typically 25 ×25 cm] than those required for use with savannah species [up to 2× 1 m]. It is thus economically feasible to deploy much larger numbers of these so-called "tiny targets" and use them to effect significant control of riverine tsetse species. In a trial in northern Uganda where tiny targets were deployed at 20 targets per linear km (giving an average density of 5.7 per sq km), it was possible to reduce the fly population by >90%. It was noted that this reduction was more than sufficient to break the transmission cycle for human African trypanosomiasis in the area (Tirados *et al.*, 2015). In the same study, experiments on islands in Lake Victoria, Kenya, suggested that tiny targets used at the above density were killing 6% of the female population per day. The suggestion is that a further increase in target density might result in the local eradication of populations, without the need to use any ancillary methods to control tsetse or trypanosomiasis.

3.7 Limitation of the study

All of the results presented here have been calculated on the assumption that, for each scenario, all rates of mortality and reproduction are constant over time. In reality, in the field, temperatures change with time and, since tsetse are poikilotherms, all of the mortality rates and developmental rates associated with reproduction also change continuously with time. The calculation of extinction probabilities is greatly complicated where temperatures are changing with time, and consideration of such

situations is beyond the scope of the current study. Extreme weather events, such as prolonged spells of very hot weather, as have been experienced in recent years in the Zambezi Valley of Zimbabwe, may push tsetse populations close to extinction. We are currently investigating the circumstances under which it is possible to calculate extinction probabilities in such situations. Where we cannot obtain analytical solutions of the type derived here, when all model parameters are time-invariant, we will use simulation methods to investigate the problem.

A full consideration of the issue of cost comparison between control methods, and the cost savings associated with eradication versus control, is an important, but complex, issue requiring full and careful consideration that is beyond the scope of the current study.

Our modelling is restricted to the calculation of extinction probabilities of populations that are closed to in and out migration. We have not attempted to extend the modelling to more complex situations where metapopulations are made up of population patches with variable inter-patch connectivity. Preliminary work suggests that extinction probabilities will be reduced in the latter situations (Peck, 2012).

3.8 Acknowledgement

The authors are extremely grateful to Professor Ekkehard Kopp for help with putting the mathematical derivations on a sound footing.

Chapter 4

Uncertainty and sensitivity analyses of extinction probabilities suggest that adult female mortality is the weakest link for populations of tsetse (*Glossina* spp.)

4.1 Abstract

Background

A relatively simple life history allows us to derive an expression for the extinction probability of populations of tsetse, vectors of African sleeping sickness. We present the uncertainty and sensitivity analysis of the extinction probability, to offer key insights into factors affecting the control or eradication of tsetse populations.

Methods

We represent tsetse population growth as a branching process, and derive closed form estimates of population extinction from that model. Statistical and mathematical techniques are used to analyse the uncertainties in estimating extinction probability, and the sensitivity of the extinction probability to changes in input parameters representing the natural life history and vital dynamics of tsetse populations.

Results

For fixed values of input parameters, the sensitivity of extinction probability depends on the baseline parameter values. Extinction probability is most sensitive to the probability that a female is inseminated by a fertile male when daily pupal mortality is low, whereas the extinction probability is most sensitive to daily mortality rate for adult females when daily pupal mortality, and extinction probabilities, are high. Global uncertainty and sensitivity analysis show that daily mortality rate for adult females has the highest impact on the extinction probability.

Conclusions

The high correlation between extinction probability and daily female adult mortality gives a strong argument that control techniques which increase daily female adult mortality may be the single most effective means of ensuring local eradication of tsetse populations.

Author summary

Tsetse (*Glossina* spp.) are vectors of African trypanosomiases, a group of deadly diseases commonly called sleeping sickness in humans and nagana in livestock. The relatively simple life history of tsetse enabled us to model its population growth as a stochastic branching process. We derived a closed-form expression for the probability that a population of tsetse goes extinct, as a function of death, birth, development and insemination rates in female tsetse. We analyzed the sensitivity of the extinction probability to the different input parameters, in a bid to identify parameters with the highest impact on extinction probability. This information can, potentially, inform policy direction for tsetse control/elimination. In all the scenarios we considered for the global sensitivity analysis, the daily mortality rate for adult females had the greatest impact on the magnitude of extinction probability. Our findings suggest that the mortality rate in the adult females is the weakest link in tsetse life history, and this fact should be exploited in achieving tsetse population control, or even eradication.

4.2 Introduction

Tsetse (*Glossina* spp.) are biting flies of both public health and economic importance in many Sub-Saharan African countries. They feed exclusively on the blood of vertebrates – game animals and livestock, and also humans, and provide the link that

drives the transmission of African trypanosomiases, tropical diseases caused by protozoan parasites of the genus *Trypanosoma*. The diseases are called sleeping sickness in humans and are caused by two sub-species of *T. brucei*. In livestock the disease is termed nagana and is caused primarily by *T. vivax* and *T. congolense*. According to a World Health Organization (WHO) 2018 factsheet for human sleeping sickness, the disease still occurs in about 36 countries in Africa, mostly among poor farmers living in rural areas. Due to sustained disease and vector control efforts, the number of cases of the sleeping sickness has declined substantially in recent years. In 2015 there were about 2804 cases recorded: 97% of these were chronic infections with *T. brucei gambiense* (World Health Organization (WHO), 2020). To sustain the reduction in cases, it is important to continue to improve understanding of the tsetse vector, in a bid to develop more effective control techniques, with improved cost effectiveness, for the control of trypanosomiasis – whether directly through the use of trypanocides, or indirectly through reducing tsetse numbers.

A recent study (Kajunguri *et al.*, 2019) employed the theory of branching processes to derive an expression for the extinction probability for closed populations of tsetse. This equation involves numerous parameters representing death, development and fertility rates during the fly's life cycle. The study made suggestions regarding the parameters of prime importance in affecting the probability of extinction. The principal aim of the present study is to take the analysis further, carrying out formal uncertainty and sensitivity analyses of all of the parameters involved in the model of population growth. Sensitivity analysis is often used to investigate the robustness of model output to parameter values (Helton *et al.*, 1985; Samsuzzoha *et al.*, 2013; Matsuyama *et al.*, 2018), but has not yet been applied to the factors affecting extinction probabilities of tsetse population.

In order to carry out these analyses, we use the branching process model developed by Kajunguri *et al.* (2019) and Hargrove (2005) for the reproductive performance of female tsetse inseminated by a fertile male. We then use a framework, developed by Harris (1965), to derive a fixed point equation for the extinction probability for a tsetse population. This approach allows us to obtain the same expression for extinction probability as Kajunguri *et al.* (2019), but it is derived with fewer steps and with less mathematical complexity. We carry out local sensitivity analysis of the extinction probability, with respect to all input parameters, at two fixed baseline values of those parameters. To identify the most important input parameters, we then use Latin Hypercube Sampling (LHS) and Partial Rank Correlation Coefficient (PRCC) methods for global uncertainty and sensitivity analyses of the extinction probability. LHS was

first applied in epidemiological modelling by Blower and Dowlatabadi (1994) (Hoare *et al.*, 2008). Several studies have since applied LHS in disease modelling, detailing its advantage over other sampling methods and describing the methodology concisely (Blower and Dowlatabadi, 1994; Sanchez and Blower, 1997; Hoare *et al.*, 2008; Kent *et al.*, 2013). PRCC has been used widely in determining the sensitivity of models of various systems (Iman *et al.*, 1981; McKay *et al.*, 2000; Kent *et al.*, 2013), especially to assess the sensitivity of disease models to various input parameters. Combining LHS and PRCC provides a robust method for assessing the uncertainty and the sensitivity of the extinction probability to all input parameters. Finally, we discuss what insights the results provide for policy makers considering the control, or local eradication of tsetse and trypanosomiases.

4.3 Materials and methods

Here we develop a stochastic model for tsetse population growth in the form of a branching process and use the model to obtain a fixed point equation for the extinction probability of tsetse populations (Kajunguri *et al.*, 2019; Hargrove, 2005; Axelrod and Kimmel, 2015). We develop the branching process focusing only on female tsetse. We follow a framework developed in Hargrove (2005), assuming a female tsetse is fertilized with probability ϵ and survives to deposit her first larva with probability $\lambda^{\nu+\tau}$: where ν is days to first ovulation, τ is the inter-larval period, and λ is the adult female daily survival probability. The pupa she produces is female with probability β, and survives to adulthood with probability ϕ^g (where g is the pupal duration and ϕ is the daily survival probability of the pupa). The mother dies before the next pregnancy, having produced a single surviving daughter, with probability $(1-\lambda^\tau)$. The probability that an adult female tsetse dies after producing a single surviving daughter after surviving one pregnancy is thus:

$$p_{1,1} = \epsilon\lambda^{\nu+\tau}\beta\phi^g(1-\lambda^\tau). \tag{4.1}$$

Equation (4.1) can be generalized by induction to obtain the probability that a female tsetse produces k surviving female offspring after surviving n pregnancies. Thus

$$p_{n,k} = \epsilon\lambda^{\nu+\tau}\binom{n}{k}\beta^n\phi^{kg}(\frac{1}{\beta}-\phi^g)^{n-k}, n>0; 1\leq k\leq n, \tag{4.2}$$

where $\binom{n}{k} = \frac{n!}{(n-k)!k!}$ is the binomial coefficient.

Suppose $p_0, p_1, p_2, ...$ are the probabilities that a female tsetse produces $0, 1, 2, ...$ surviving female offspring in her lifetime, respectively. Suppose also that $p_0 + p_1 < 1$,

to avoid the trivial case where a tsetse fly only produces 0 or 1 female offspring. Summing equation (4.2) over all n, gives p_k, the probability that a female produces k surviving female offspring in its lifetime.

$$p_k = \frac{\epsilon\lambda^{\nu+\tau}(1-\lambda^\tau)\beta^k\phi^{kg}}{(1-\beta\lambda^\tau(\frac{1}{\beta}-\phi^g))^{k+1}}, k > 0. \tag{4.3}$$

Equation (4.3) was used in Kajunguri *et al.* (2019) to obtain the mean and variance of the population size, extinction probability and time to extinction of populations of tsetse. Proofs of equations (4.1) and (4.2) are provided in Kajunguri *et al.* (2019) (Supplementary Information).

It can be shown easily that $p_0, p_1, p_2, ...$ follow a geometric series, such that $p_k = bc^{k-1}$, $k = 1, 2, 3, ...$, where $b, c > 0$; and $p_0 = 1 - \sum_{i=1}^{\infty}$. Equation (4.3) then becomes:

$$p_k = \frac{\epsilon\lambda^{\nu+\tau}(1-\lambda^\tau)\beta\phi^g}{(1-\beta\lambda^\tau(\frac{1}{\beta}-\phi^g))^2}(\frac{\beta\phi^g\lambda^\tau}{(1-\beta\lambda^\tau(\frac{1}{\beta}-\phi^g)}\Big)^{k-1}, \tag{4.4}$$

where $b = \frac{\epsilon\lambda^{\nu+\tau}(1-\lambda^\tau)\beta\phi^g}{(1-\beta\lambda^\tau(\frac{1}{\beta}-\phi^g))^2}$ and $c = \frac{\beta\phi^g\lambda^\tau}{(1-\beta\lambda^\tau(\frac{1}{\beta}-\phi^g)}$.

Following a framework developed in Harris (1965), the generating function $g(\theta)$ of p_k, is a fractional linear function given by;

$$g(\theta) = 1 - \frac{b}{(1-c)} + \frac{b\theta}{1-c\theta}, 0 \leq \theta \leq 1. \tag{4.5}$$

4.3.1 Extinction probability

The extinction probability for tsetse population is the non-negative fixed point of equation (4.5), i.e. $0 \leq \theta \leq 1$ such that $g(\theta) = \theta$.

$$\theta = \frac{1-\lambda^\tau(1-\beta\phi^g(1-\epsilon\lambda^\nu))}{\beta\phi^g\lambda^\tau}, \tag{4.6}$$

where $\beta\phi^g\lambda^\tau \neq 0$. In practice, $0 < \beta < 1$, $0 < \lambda < 1$ and $0 < \phi < 1$. In other words, the survival probabilities for both adult females and female pupa, and the probability that a pupa deposited is female are all in the open interval $(0, 1)$. This allows us to avoid the trivial cases where $\theta = 0$ or $\theta = 1$. Equation (4.6) is the solution for the situation where the initial population consists of just a single female fly. For N flies in the pioneer population, and assuming that the survival and reproductive rates of all individual flies are independent, the extinction probability is θ^N.

4.3.2 Local sensitivity analysis of θ

In this section, we perform local sensitivity analysis, otherwise known as elasticity analysis, on the extinction probability for tsetse populations. Given that the extinction

probability θ, depends differentiably on each input parameter, the normalized forward sensitivity (elasticity) index of θ with respect to all input parameters is:

$$\Pi^{\theta}_{\rho_i} = \frac{\rho_i}{\theta}\frac{\partial\theta}{\partial\rho_i}, i = 1, 2, ..., 7, \tag{4.7}$$

where ρ_i is the set of all input parameters of the extinction probability. This method has been used extensively in the literature to determine the sensitivity of the reproduction number R_0 of epidemiological models to model parameters (Chitnis *et al.*, 2008; Samsuzzoha *et al.*, 2013; Matsuyama *et al.*, 2018). When the initial population consists of N female tsetse, the extinction probability is θ^N. The sensitivity indices of θ^N with respect to all input parameters is;

$$\Pi^{\theta^N}_{\rho_i} = \frac{\rho_i}{\theta^N}\frac{\partial\theta^N}{\partial\rho_i} = N\frac{\rho_i\theta^{N-1}}{\theta^N}\frac{\partial\theta}{\partial\rho_i} = N\frac{\rho_i}{\theta}\frac{\partial\theta}{\partial\rho_i} = N\Pi^{\theta}_{\rho_i}. \tag{4.8}$$

Notice that, when there are N female flies in the initial population, the sensitivity indices of θ^N for all input parameters is the sensitivity indices of θ multiplied by N. The larger the size of the initial population, the more sensitive extinction probability is to input parameters.

Writing equation (4.6) in terms of the daily mortality rate for adult females (ψ), and the daily mortality rate for female pupae (χ), yields:

$$\theta = \frac{1 - \left(e^{-\psi}\right)^{\tau}\left(1 - \beta\left(e^{-\chi}\right)^{g}\left(1 - \epsilon\left(e^{-\psi}\right)^{\nu}\right)\right)}{\left(e^{-\psi}\right)^{\tau}\left(e^{-\chi}\right)^{g}\beta}. \tag{4.9}$$

Table 5.1 shows the derivations of the sensitivity indices of extinction probability with respect to all seven input parameters. These expressions were derived from equations (4.7) and (4.9) with a simple code in MAPLE 17 environment.

4.4 Results

Table 4.2 shows the sensitivity indices of extinction probability for each input parameter at different values of extinction probabilities. For instance, the sensitivity index of θ with respect to ϵ (probability female is inseminated by a fertile male) decreases by $> 60\%$ when θ (extinction probability) approaches 1. Thus, at $\theta = 0.419$, a 10% decrease in ϵ yields only a 22% increase in θ, whereas, at $\theta = 0.96$, a 10% decrease in ϵ will only yield an 8.7% increase in θ.

Table 4.1: Expressions for the sensitivity indices of extinction probability for each parameter.

Parameters	The sensitivity of extinction probability (θ) to input parameters
β: Probability deposited pupa is female	$\Pi_{\beta}^{\theta} = -\frac{-1+\left(e^{-\psi}\right)^{\tau}}{-1+\left(e^{-\psi}\right)^{\tau}-\left(e^{-\psi}\right)^{\tau}(e^{-\chi})^{g}\beta+\left(e^{-\psi}\right)^{\tau+\nu}(e^{-\chi})^{g}\beta\,\epsilon}.$
χ: Daily pupal mortality	$\Pi_{\chi}^{\theta} = \frac{\chi\, g\left(-1+\left(e^{-\psi}\right)^{\tau}\right)}{-1+\left(e^{-\psi}\right)^{\tau}-\left(e^{-\psi}\right)^{\tau}(e^{-\chi})^{g}\beta+\left(e^{-\psi}\right)^{\tau+\nu}(e^{-\chi})^{g}\beta\,\epsilon}.$
ϵ: Probability of insemination	$\Pi_{\epsilon}^{\theta} = \frac{\left(e^{-\psi}\right)^{\tau+\nu}\left(e^{-\chi}\right)^{g}\beta\,\epsilon}{-1+\left(e^{-\psi}\right)^{\tau}-\left(e^{-\psi}\right)^{\tau}(e^{-\chi})^{g}\beta+\left(e^{-\psi}\right)^{\tau+\nu}(e^{-\chi})^{g}\beta\,\epsilon}.$
g: Pupal duration	$\Pi_{g}^{\theta} = \frac{\chi\, g\left(-1+\left(e^{-\psi}\right)^{\tau}\right)}{-1+\left(e^{-\psi}\right)^{\tau}-\left(e^{-\psi}\right)^{\tau}(e^{-\chi})^{g}\beta+\left(e^{-\psi}\right)^{\tau+\nu}(e^{-\chi})^{g}\beta\,\epsilon}.$
ψ: Daily adult mortality	$\Pi_{\psi}^{\theta} = -\frac{\psi\left(\left(e^{-\psi}\right)^{\tau+\nu}\left(e^{-\chi}\right)^{g}\beta\,\epsilon\,\nu+\tau\right)}{-1+\left(e^{-\psi}\right)^{\tau}-\left(e^{-\psi}\right)^{\tau}(e^{-\chi})^{g}\beta+\left(e^{-\psi}\right)^{\tau+\nu}(e^{-\chi})^{g}\beta\,\epsilon}.$
τ: Inter-larval period	$\Pi_{\tau}^{\theta} = \frac{\tau\,\ln\left(e^{-\psi}\right)}{-1+\left(e^{-\psi}\right)^{\tau}-\left(e^{-\psi}\right)^{\tau}(e^{-\chi})^{g}\beta+\left(e^{-\psi}\right)^{\tau+\nu}(e^{-\chi})^{g}\beta\,\epsilon}.$
ν: Time from female emergence to first ovulation	$\Pi_{\nu}^{\theta} = \frac{\nu\,\beta\left(e^{-\chi}\right)^{g}\left(e^{-\psi}\right)^{\tau+\nu}\epsilon\,\ln\left(e^{-\psi}\right)}{-1+\left(e^{-\psi}\right)^{\tau}-\left(e^{-\psi}\right)^{\tau}(e^{-\chi})^{g}\beta+\left(e^{-\psi}\right)^{\tau+\nu}(e^{-\chi})^{g}\beta\,\epsilon}.$

4.4.1 Varying sensitivity indices of θ for all input parameters as a function of χ

Here we investigate the changes that occur in the sensitivity indices of extinction probability for six input parameters as we vary χ, the daily mortality rate in female pupae. A script was written in MAPLE 17 environment to calculate the local sensitivity indices of θ with respect to the six remaining input parameters for different values of χ. Figure 4.1 shows changes in the sensitivity indices of θ with respect to each parameter as the daily mortality rate for female pupae (χ) varies from 0.1% to 2.5%, while keeping the other baseline values constant (Table 4.2).

Table 4.2: List and description of parameters affecting extinction probabilities for tsetse populations, and the sensitivity indices for these parameters, at two different values of extinction probability.

Parameters & descriptions	Baseline values	Sensitivity indices $\theta = 0.419$	$\theta = 0.960$
Daily mortality rate for adult females ($\psi = -\ln(\lambda)$)	0.02-0.03 per-day (Lord *et al.*, 2018)	+1.030	+1.080
Daily mortality rate for female pupae ($\chi = -\ln(\phi)$)	0.01-0.025 per-day (Lord *et al.*, 2018)	+0.507	+0.374
Probability deposited pupa is female (β)	0.5 (Hargrove, 2005)	-0.836	-0.832
Probability female is inseminated by a fertile male (ϵ)	1 (Hargrove, 2005)	-2.220	-0.870
Inter-larval period (τ)	9 days (Hargrove, 2005)	+0.875	+0.929
Pupal duration (g)	27 days (Hargrove, 2005)	+0.507	+0.374
Time from adult female emergence to first ovulation (ν)	7 days (Hargrove, 2005)	+0.158	+0.154

As χ increases from 0.001 to 0.0065, the sensitivity index of θ with respect to ϵ reduces below the sensitivity index of θ with respect to ψ. At that point extinction probability becomes more sensitive to ψ than ϵ. When χ increases further to 0.013, the sensitivity of extinction probability to ϵ drops further below the sensitivity of extinction probability to τ (Fig 4.1).

4.4.2 The performance of different control approaches when used in combination

The inter-dependence of sensitivity indices evident in Figure 4.1 suggests the need to consider the effects on the dynamics of a tsetse eradication campaign of using more than one control technique simultaneously. Accordingly, we estimated the times to extinction for various combinations of parameters affecting rates of mortality and reproduction. For example, the recently proposed Boosted SIT (BSIT) method would see sterile males treated also with the juvenile hormone analogue pyriproxyfen (Laroche, 2017; Laroche *et al.*, 2018), which would see simultaneous decreases in pupal production, and increases in the mortality of those pupae that are produced. As expected, for given level of sterile mating, the time to extinction decreases as pupal mortality increases. This effect is also impacted by the background level of adult female mortality (ψ) (Fig 4.2A, B). For example, if $1-\epsilon = 0.9$ and $\psi = 1\%$ per day, the expected times to extinction of a pioneer population of 1000 female tsetse are 4.9 and 2.2 generations when pupal mortalities are 1% per day, or 6% per day, respectively (Fig 4.2A). Adding

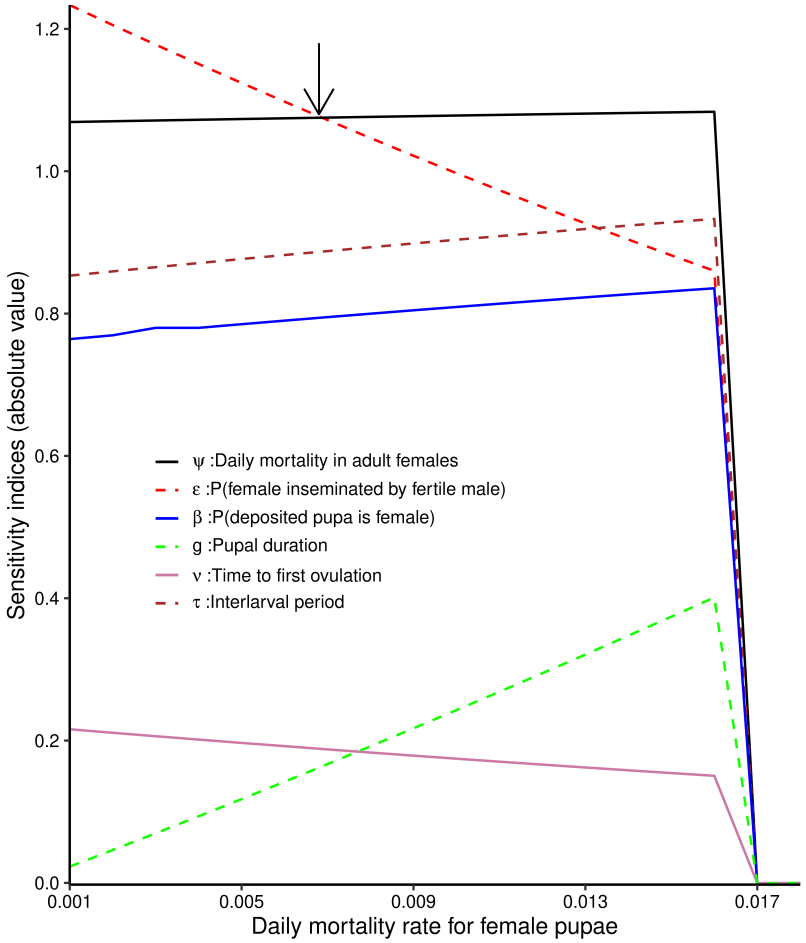

Figure 4.1: Variation in the sensitivity of extinction probability θ to six input parameters (β, ϵ, ν, g, ψ, τ) as a function of the values of the background daily rate (χ) of female pupal mortality. The sensitivity indices of extinction probability to six input parameters, in absolute value. The arrow through the plot indicates the point where θ becomes more sensitive to ψ than ϵ.

the extra pupal mortality thus reduces the time to extinction by 2.7 generations, or 55.1%. The difference is much smaller, however, when $\psi = 5$ % per day: now the times to extinction are 1.7 and 1.1 generations, respectively, for the above levels of pupal mortality (Fig 4.2B).

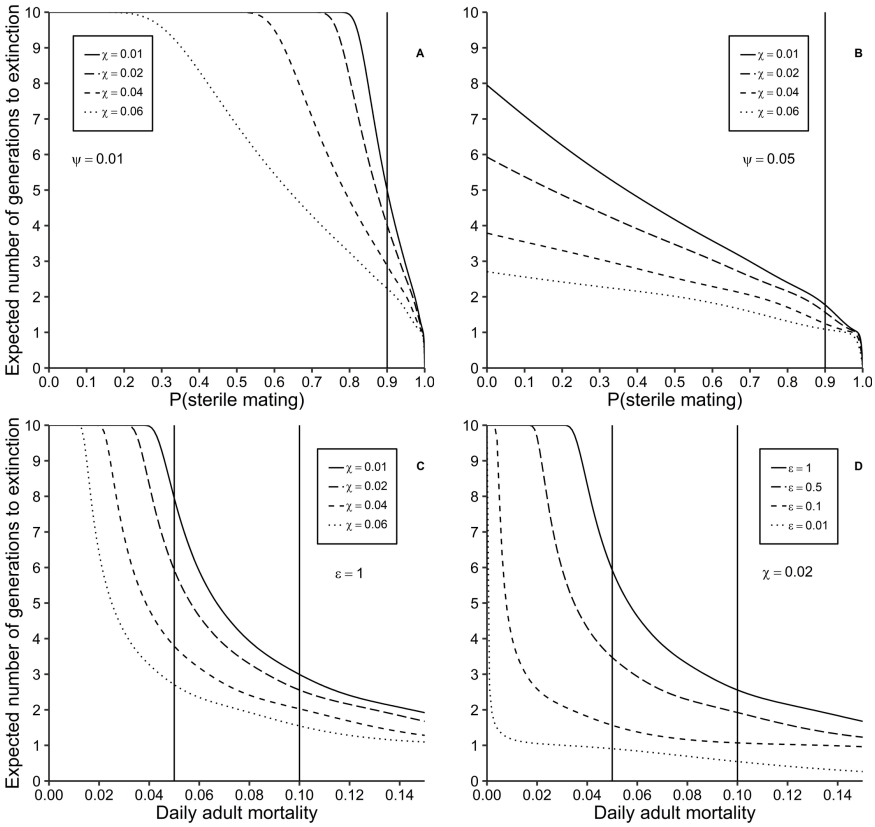

Figure 4.2: Expected number of generations to extinction as a function of various input parameters. Expected number of generations to extinction as a function of: A. The probability (1-ϵ) of sterile mating for different levels of daily pupal mortality (χ), at daily adult mortality $\psi = 1\%$ B. The probability of sterile mating for different levels of daily pupal mortality, at daily adult mortality = 5%. C. Daily adult mortality for different levels of daily pupal mortality, and with no sterile mating: $\epsilon = 1$. D. Daily adult mortality for different levels of probability of insemination, at daily pupal mortality = 2%

When the primary focus of the control is to kill adult females, as when using insecticide-treated targets for example, the advantage of killing pupae simultaneously is small when adult mortality is of the order of ψ= 10% per day – as is the case for the use of targets against *G. pallidipes* (Vale *et al.*, 1986). In that case the time to extinction is only 2.9 generations even with a background pupal mortality of $\chi = 1\%$ per day (Fig 4.2C), declining only slightly to 1.5 generations if χ is increased to 6% per day. When $\psi = 5\%$ per day, the difference is greater: 7.9 and 2.7 generations for $\chi = 1\%$ and 6%, respectively.

A similar picture emerges when adult killing is combined with the sterilisation of adult females (Fig 4.2D). When ψ= 10 % per day, the expected time to extinction is only 2.6 generations – even without the release of any sterile males ($\epsilon = 1$). If the population is flooded to the point where sterile males outnumber the wild males by 100:1 ($\epsilon = 0.01$), 0.5 generations are required to achieve extinction, a difference of only

2.1 generations. When $\psi = 5\%$ per day the decrease is more substantial – from 5.9 to 0.9 generations as ϵ decreases from 1 to 0.01 (Fig 4.2D).

4.4.3 Global uncertainty and sensitivity analysis of θ

As the above results indicate, local sensitivity analysis may not be may not be sufficient to capture the influence of all input parameter values on the extinction probability since there are interdependencies between input parameters. Accordingly, we also carried out global uncertainty and sensitivity analysis of the extinction probability for tsetse population.

The precise values of the input parameters are not known in field situations, where many of these parameters depend on temperature and other climatic factors. It is therefore important to quantify the uncertainty involved in estimating the extinction probability (θ). To achieve this, and to establish the most important input parameters, we use LHS and PRCC methods for the global uncertainty and sensitivity analysis of the extinction probability. The method follows the approach of Samsuzzoha *et al.* (2013).

4.4.3.1 Uncertainty analysis

We analyse the uncertainty involved in quantifying extinction probability (θ) based on the uncertainties associated with the input parameters. Accordingly, in order to investigate the sensitivity to this uncertainty we sample values from distributions of these parametes. We define prior probability distribution functions for each of the input parameters, based on the studies done on the life cycle of tsetse published in the literature (Lord *et al.*, 2018; Phelps and Burrows, 1969*b*). The probability distribution functions are given in Table 4.3, where β, N and U denote beta, normal and uniform distributions, respectively. The vast majority of studies on which the parameters are based were carried out on *G. m. morsitans* Westwood, but the limited information available from the literature suggests that there are relatively minor differences, between species, in the rates of pupal production and development (Challier, 1982).

Table 4.3: List of parameters and their prior probability distributions .

Parameters	Prior probability distribution
ψ	$\beta(0.4, 12)$
χ	$\beta(0.3, 12)$
β	$N(0.5, 0.01)$
τ	$N(9, 0.747)$
g	$N(30, 1)$
ν	$N(8, 0.011)$

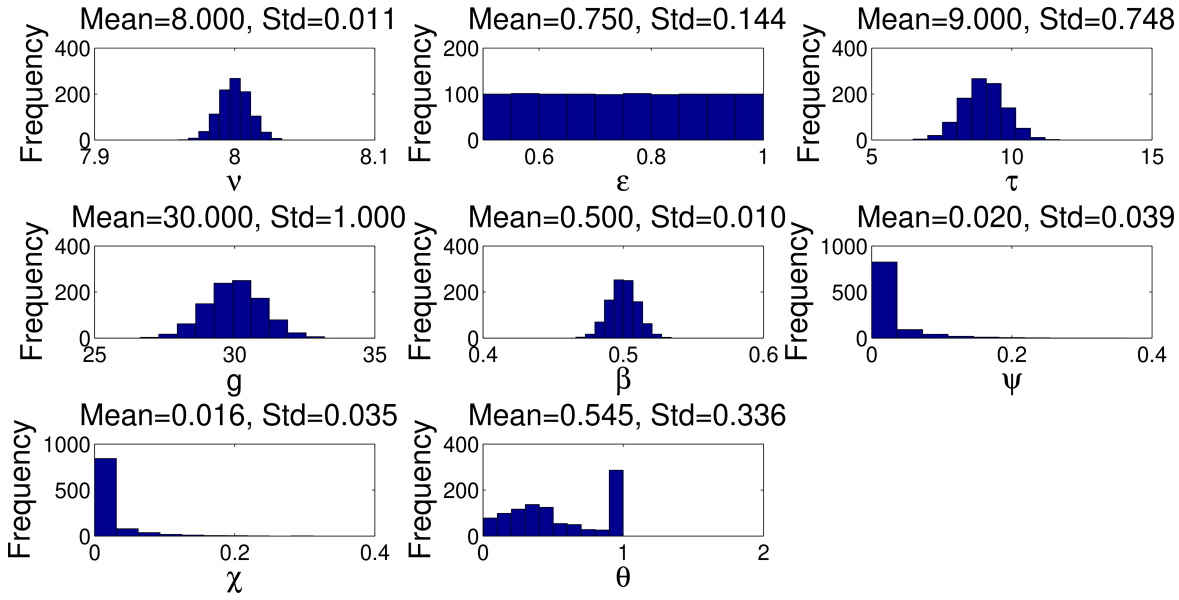

Figure 4.3: The uncertainty output for all input parameters, together with uncertainty output of the extinction probability, obtained from Latin hypercube sampling using a sample size of 1000 for the seven input parameters. β is the probability deposited larva is female, ϵ probability female is inseminated by a fertile male, g the pupal duration and ν time from female emergence to first ovulation, τ is the inter-larval period, χ the daily mortality rate for female pupae, ψ is the daily mortality rate for females and θ the extinction probability.

Moreover, given that the qualitative aspects of the life history are identical for all species of *Glossina*, and that unit changes in pupal or adult mortality will affect various species in the same quantitative manner, we can be confident that the equations developed here will apply to all species. What will differ, in ways that we are not currently in a position to judge, is the quantitative effect of changes in climate, and other aspects of the environment, on the survival and reproductive rates in different

species of *Glossina*. More work is necessary, particularly on forest and riverine species, to elucidate the relationship between environmental variables and rates of mortality and reproduction in tsetse.

Using LHS, we obtain the uncertainty output for all the input parameters and also for the extinction probability. LHS is used to sample from the stratified probability distribution functions for different parameters, using 1000 intervals of equal probabilities. Figure 4.3 shows the uncertainty output for all the input parameters and the shape of their probability distribution, together with their summary statistics. The uncertainty output for extinction probability (θ) shows that it is beta distributed with mean = 0.545 and standard deviation = 0.336.

4.4.4 PRCC/sensitivity indices of θ with respect to all input parameters

To identify key input parameters, we carry out a sensitivity analysis by calculating the PRCC between each input parameter and the extinction probability. The parameter with the highest PRCC has the largest influence on the magnitude of the extinction probability. Figure 4.4 shows the PRCC outputs for all input parameters, where the probability (ϵ) that a female fly is inseminated by a fertile male is essentially equal to 1. In the field, males manage to find and mate with females, even at vey low population levels (Glasgow, 1963). For most tsetse populations, therefore, the probability of insemination is likely close to 1. Accordingly, we allow ϵ to vary between 0.999-1. In Figure 4.4B, the prior probability distributions are kept the same, save for ϵ which is sampled between 0.885 and 1 (Blower and Dowlatabadi, 1994; Sanchez and Blower, 1997; Chowell *et al.*, 2004).

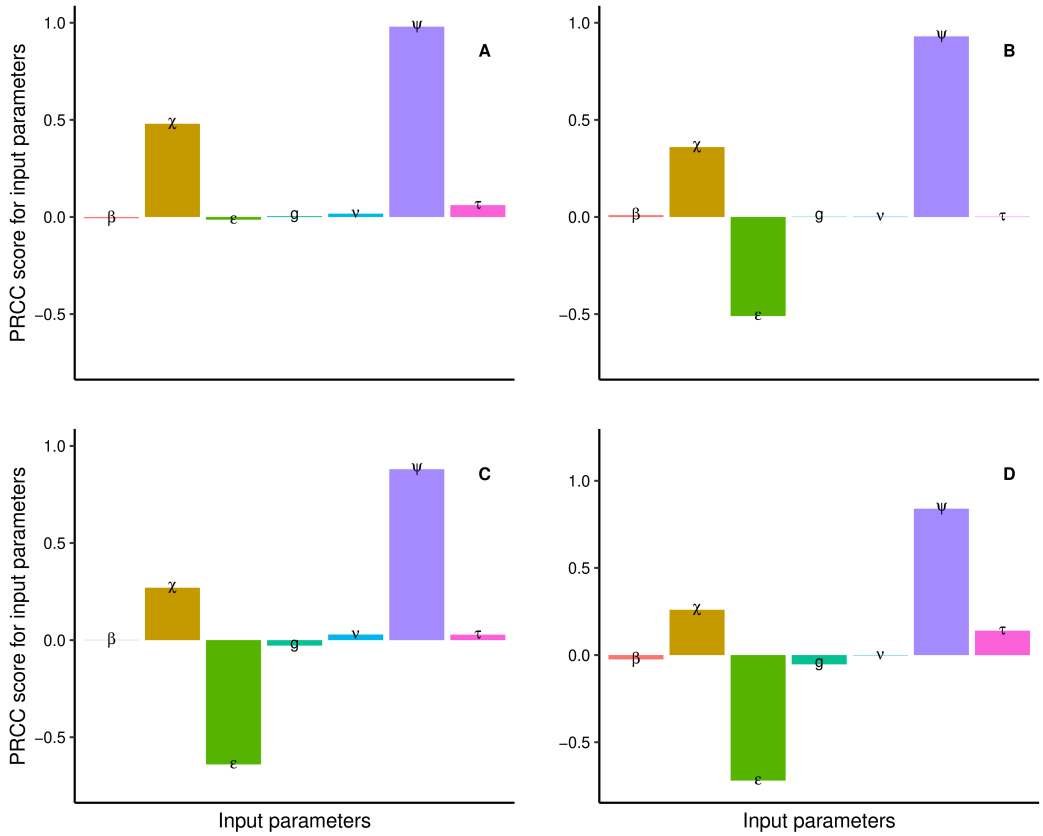

Figure 4.4: PRCC output for all input parameters with respect to the extinction probability. (A). Sampling ϵ between 0.999 and 1. (B). Sampling ϵ between 0.855 and 1. (C). Sampling ϵ between 0.51 and 1. (D). Sampling ϵ between 0.1 and 1. ψ is the daily mortality rate for females, χ the daily mortality rate for female pupae, β the probability deposited larva is female, ϵ probability female is inseminated by a fertile male, τ the inter-larval period, g pupal duration and ν time from female emergence to first ovulation

LHS is used to sample from the prior probability distributions, where ϵ is sampled from a uniform distribution $U(0.999, 1)$. Figure 4.4A shows that daily mortality rate for adult females (ψ) has a strong correlation with the extinction probability with PRCC score 0.91, followed by daily mortality rate for female pupae (χ) and inter-larval period (days) (τ), with PRCC scores of 0.47 and 0.058, respectively.

The female tsetse generally mates only once in her lifetime, storing the sperm in spermathecae and using small amounts to fertilize her eggs one at a time (Madsen *et al.*, 2013; Alderton *et al.*, 2018). When sterile males are introduced into a tsetse population, the probability (ϵ) that a female is inseminated by a fertile male falls below unity, by an amount that depends on the ratio of sterile to fertile males in the population.

The Sterile Insect Technique (SIT) has been used in attempts to control tsetse populations (Takken and Weiss, 1978; Abd-Alla *et al.*, 2013) and was used to locally eradicate a small population of *G. austeni* on Unguja Island, Zanzibar, Tanzania (Vreysen *et al.*, 2000). The probability that a female is inseminated by a sterile male is $1 - \epsilon$. We allowed baseline values of ϵ to vary over a wide range, in order to assess the sensitivity of extinction probability to changes in ϵ, at varying baseline levels of the proportions of sterile males in the population. Figure 4.4 show the PRCC scores when ϵ is uniformly distributed either as U(0.855, 1), U(0.51, 1) or U(0.1, 1). The PRCC scores for ϵ in these three scenarios were -0.51, -0.64 and -0.72, respectively. Thus the absolute value of the PRCC score for ϵ increases as we allow more variability in the probability distribution function.

4.5 Discussion

The simple life history of the tsetse enabled us to model its population dynamics as a stochastic branching process. We derived an expression for the extinction probability for tsetse populations and performed local and global sensitivity analyses, as well as global uncertainty analysis, on the extinction probability. We calculated all results for two fixed baseline values for χ, the pupal mortality rate, corresponding to values that resulted in low or high extinction probabilities. We obtained the sensitivity indices of the extinction probability to seven input parameters. When the extinction probability (θ) is fixed at either low or high levels (0.419 or 0.960), θ is more sensitive to changes in daily adult mortality (ψ) and the fertile insemination probability (ϵ) than to any of the other parameters. For a change in θ from 0.419 to 0.960, the sensitivity index of θ with respect to ψ increases by 0.05, whereas the change with respect to ϵ is larger, at 1.35 (decrease in absolute value) (Table 4.2). The parameters ψ and ϵ are important as they underpin the two main approaches to tsetse control. Hocking et al (Hocking *et al.*, 1963) broadly classified tsetse control and elimination techniques including game destruction, bush clearing, use of insecticides and biological control. These techniques can be pooled into two fundamental control philosophies - those which aim, primarily, to increase mortality rates in adult flies (corresponding to our ϕ) and those, like SIT, which aim to reduce tsetse birth rates (corresponding to our proportion of female inseminated, ϵ) (Takken and Weiss, 1978). Our sensitivity analysis indicates which parameter out of the two has the highest impact on the extinction probability.

From Table 4.2, observe that the sensitivity indices of θ to the input parameters depend on the value of the extinction probability. We allowed the daily mortality rate

for pupae (χ) to vary from 0.001 to 0.025. The lower and upper bound values result in low and high extinction probabilities, respectively. We then calculated the sensitivity indices of θ with respect to the remaining six parameters. Figure 4.1 shows that the sensitivity of θ to each of the input parameters changes as extinction probability increases with increasing values of χ. Observe that for $\chi \geq 0.018$, the sensitivity indices of all the six parameters converged to zero. This is expected since the set baseline parameters values for all input parameters correspond to an extinction probability $\theta = 1$ at $\chi \geq 0.018$. This can be verified easily, by substituting parameter values into equation (4.6).

LHS and PRCC provide a suitable technique for assessing the impact of input parameters on the output and therefore inform possible choices for effective control efforts (Marino *et al.*, 2008). We defined prior probability density functions for the seven input parameters and we sampled from intervals of equal probability using LHS. The PRCC score of all input parameters was obtained for three sets of the probability distribution function, fixed for six parameters and varied only for ϵ. In all cases, ψ has the strongest impact on the extinction probability. The PRCC score for ϵ increases as we allow for more variability in its prior probability distribution.

The effectiveness of SIT is highly dependent on the daily mortality rates for female pupae. As the daily mortality for female pupae increases, extinction probability becomes less and less sensitive to the probability a female is inseminated by a fertile male (Fig 4.1). In contrast, the sensitivity of extinction probability to daily female mortality is almost constant, regardless of the daily mortality rates for female pupae. Previous theoretical studies and practical control campaigns have established the prime importance of increasing adult female mortality as a means of achieving local elimination of tsetse and trypanosomiases (Kajunguri *et al.*, 2019; Vale *et al.*, 1988*b*). Our sensitivity analysis supports this conclusion and shows how the probability of extinction varies with small changes in adult mortality. A maximum daily birth rate of about 3% per day in tsetse means that as death rates – whether natural or imposed – exceed 3%, population numbers decline at an increasingly rapid pace. This will be true for all tsetse, whether savannah, riverine or forest species. What is less clear is the extent to which it is possible, for different species of tsetse, to impose the required increases in mortality.

A single insecticide-treated target baited with acetone and 1-octen-3-ol kills 0.5% and 2.5%, respectively, of adult female *G. m. morsitans* and *G. pallidipes* (Vale *et al.*, 1988*b*). The later identification of two attractive phenols and improved target design,

led to an approximate doubling of target efficacy for the above species (Saini and Hassanali, 1992; Vale, 1993; Vale and Torr, 2004). If used at a density of 4 targets per sq km this would result in mortalities of 2% and 10%, respectively, for adult female *G. m. morsitans* and *G. pallidipes*.

Riverine tsetse, such as *G. palpalis* and *G. fuscipes*, depend much less on odor for the detection of hosts. Smaller proportions of a population can therefore be attracted to an individual trap or target. These flies will, however, approach much smaller targets (7% of surface area of targets used for savannah tsetse) unaccompanied by odor. For *G. f. fuscipes* it is estimated that each of these so-called "tiny target" kills 0.2-0.3% per day of adult females (Tirados *et al.*, 2015). The targets are so cheap that they can be produced in huge numbers, and so small that they can be easily and rapidly deployed. Used at an appropriate density they can thereby provide a sufficient increase in mortality among riverine tsetse that vector control could be an important component of the elimination of Gambian sleeping sickness (Vale *et al.*, 2015; Lehane *et al.*, 2016).

Similarly, insecticide treated cattle have been used to good effect in the control of trypanosomiasis in many situations, including those where riverine flies are the vectors, for example in controlling Rhodesian sleeping sickness in Uganda (Welburn and Coleman, 2015). We may thus be confident that our sensitivity analyses support the idea that, for both savannah and riverine flies, it is possible to envisage increasing adult female mortality to the point where tsetse can be locally eliminated.

As illustrated in this study, and previously, tsetse population growth rate is also very sensitive to changes in the probability that an adult female is inseminated by a fertile male. This suggests alternative approaches to vector control, aimed at reducing the birth rate. In practice this currently involves SIT. It is, however, agreed that SIT cannot practically be used as a stand-alone technique to achieve tsetse eradication. Instead, it can be used against small remnant populations following major reductions in fly numbers achieved using insecticidal techniques (Vreysen *et al.*, 2000). In the event that local eradication can be achieved using only the insecticidal technique then this will, of course, save the large extra cost due to an additional SIT operation. This situation arose, for example, in the elimination of *G. m. morsitans*, using odor-baited targets, from the Umfurudzi wildlife area in Zimbabwe (Hargrove, 2003*b*) and of *G. m. centralis*, using aerial spraying, from the Okavango Delta of Botswana (Kgori *et al.*, 2006). In neither case was it necessary or desirable to use SIT.

Laroche has recently suggested a new approach, termed Boosted SIT (BSIT), where sterile male tsetse are treated with the juvenile hormone analogue, pyriproxyfen, prior to release (Laroche, 2017; Laroche *et al.*, 2018). Treating adult tsetse with pyriproxyfen does not affect their survival, but treated females produce larvae that die before they complete development. This has been demonstrated in the laboratory and in the field (Langley *et al.*, 1988, 1990; Hargrove and Langley, 1990, 1993). The idea behind BSIT is that the sterile males released would affect the wild tsetse population in two ways. First, virgin females with which they mate successfully do not produce any larvae. In terms of our model, ϵ decreases. Second, even if the male fails to mate with the female, transfer of pyriproxyfen to the female results in the death of any pupae produced. In terms of our model, χ increases. BSIT would thus result in simultaneous decreases in the probability of successful insemination, and increases in pupal mortality. Our sensitivity analysis shows, however, that as χ increases, there is a sharp decrease in the absolute value of the sensitivity index for ϵ (Figure 4.1). That is to say, increases in the efficacy of pyriproxyfen results in a decreased efficacy of SIT. From Figure 4.2 it is also clear that, in a situation where sterile males are released to the point where (1-ϵ) = 0.9, increasing adult female mortality (ψ) has a bigger impact on the time to extinction than increasing pupal mortality (χ). Thus, when ψ= 0.01 the time to extinction is 2.2 generations, even when χ is increased to 0.06. When ψ is increased to 0.05, however, the period is even shorter at 1.7 generations – even when pupal mortality χ is only 0.01. More careful analysis will thus be required to judge the extent to which the combined use of SIT and pyriproxyfen (i.e. BSIT) changes efficacy and cost effectiveness - and the relative merits of this approach and the simultaneous use of SIT and insecticide-treated targets.

Notice that the above problem does not occur for interventions where adult female tsetse are killed: increases in pupal mortality result only in a slight increase in the absolute value of the sensitivity index of ψ, the adult female mortality (Figure 4.1). There would thus be a simple additive effect of killing pupae as well as adult females. Nobody has, however, suggested a suitable means of combining these two killing methods. Using both insecticide and a juvenile hormone analogue, such as pyriproxyfen, on the same target makes little sense. As long as the insecticide is effective the presence of the pyriproxyfen would be irrelevant.

4.6 Conclusions and limitations

In all scenarios considered in the global sensitvity analysis of extinction probability, control techniques which can achieve high mortality rates for adult female flies have the strongest impact on extinction probability. SIT, which can reduce reproductive rates, without increasing mortality, can also have a strong impact on extinction probability – but cannot be used as stand-alone method for achieving local tsetse eradication. Where insecticidal approaches, such as aerial spraying, or insecticide-treated targets/cattle, can be used by themselves to achieve tsetse local extinction, this will save the extra expense of adding the SIT component.

The major limitation of our approach is that it is necessarily a simplification of real situations. For example, our modelling framework assumes that the population is unperturbed by movements between tsetse patches. In other words, the population is closed, such that, when tsetse populations are depleted, they cannot be replenished by invading tsetse from neighbouring patches. Finally, our work is based on the assumption that tsetse experience fixed environmental conditions throughout their life history. This assumption is not true in the wild, where tsetse experience daily and seasonal changes in various climatic effects. In future work we will estimate extinction probabilities for flies experiencing the variable climatic conditions typical of field situations.

4.7 Acknowledgment

The authors would like to show their gratitude to Dr. Carl Pearson for his insightful review of the first draft of this article.

Chapter 5

Extinction probabilities as a function of temperature for populations of tsetse (*Glossina* spp.)

5.1 Abstract

Significant reductions in populations of tsetse (*Glossina* spp.) in parts of Zimbabwe have been attributed to increases in temperature over recent decades. Sustained increases in temperature might lead to local extinctions of tsetse populations. Extinction probabilities for tsetse populations have not so far been estimated as a function of temperature. We develop a time-homogeneous branching process model for situations where tsetse live at different levels of fixed temperature. We derive a probability distribution $p_k(T)$ for the number of female offspring an adult female tsetse is expected to produce in her lifetime, as a function of the fixed temperature at which she is living. We show that $p_k(T)$ can be expressed as a geometric series: its generating function is therefore a fractional linear type. We obtain expressions for the extinction probability, reproduction number, time to extinction and growth rates. The results are valid for all tsetse, but detailed effects of temperature will vary between species. No *G. m. morsitans* population can escape extinction if subjected, for extended periods, to temperatures outside the range 16°C-32°C. Extinction probability increases more rapidly as temperatures approach and exceed the upper and lower limits. If the number of females is large enough, the population can still survive even at high temperatures (28°C-31°C). Small decreases or increases in constant temperature in the neighbourhoods of 16°C and 31°C, respectively, can drive tsetse populations to extinc-

tion. Further study is needed to estimate extinction probabilities for tsetse populations in field situations where temperatures vary continuously.

Author summary

Tsetse (*Glossina* spp.) are the vectors of the African sleeping sickness. We derived expressions for the extinction probability, and mean time to extinction, of closed populations of *G. m. morsitans* experiencing different levels of fixed temperature. Temperature plays a key role in tsetse population dynamics: no population of *G. m. morsitans* can escape extinction at constant temperatures < 16°C or > 32°C. The effect of temperature is more severe if tsetse populations are already depleted. Increasingly high temperatures due to climate change may alter the distribution of tsetse populations in Africa. The continent may witness local extinctions of tsetse populations in some places, and appearances in places hitherto too cold for tsetse.

5.2 Introduction

A bite from a tsetse (*Glossina* spp.) infected with a parasite of the genus *Trypanosoma* may cause human African trypanosomiasis (HAT), commonly called sleeping sickness in humans, or animal African trypanosomiasis (AAT), commonly called nagana in livestock. These tropical diseases have ravaged the African continent for centuries. They pose serious public health and socio-economic problems, especially to rural farmers, who rely on their livestock for daily subsistence, draught power and general economic gain. Sleeping sickness is difficult to diagnose and the treatments are often difficult to administer (Lejon *et al.*, 2013). Vector control can play an important role in the fight against the trypanosomiases (Solano *et al.*, 2013), and understanding the population dynamics of the vector is thus crucial for the control or elimination of both sleeping sickness and nagana.

As with all insects, the body temperature of tsetse is largely determined by ambient temperature and all of the flies' physiological processes are determined by the temperatures that they experience. Tsetse use various behavioural devices to mitigate the effects of extreme ambient temperatures, such that the temperatures they actually experience are less extreme than indicated by temperatures measured in, for instance, a Stevenson screen (Vale, 1971; Muzari and Hargrove, 2005). Nonetheless, excessively high, or low, temperatures are lethal for them (Phelps and Clarke, 1974; Ackley and Hargrove, 2017). This is a serious concern for tsetse because, unlike other insects, the

genus *Glossina* is characterized by birth rates that do not exceed about 4% per day. It follows that, for mortality rates $> 4\%$ per day, mortality exceeds natality, resulting in negative growth rates for tsetse populations. If these negative rates are sustained the tsetse population will be driven to extinction. In theory, therefore, tsetse populations should be relatively easy to control, or even locally eradicate, using strategies that achieve quite modest increased mortalities. Equally, regional extinction could result from increases in mortality consequent on environmental changes, including increases in temperature.

As an example of this effect, a study published in 2018 concluded that, over the previous 40 years, there had been a significant increase in temperatures in the Zambezi Valley of Zimbabwe (Lord *et al.*, 2018). Specifically, peak temperatures at Rekomitjie Research Station increased by c. 0.9°C from 1975 to 2017, with an increase of c. 2°C at the hottest time of the year (October-November). These increases in temperature were associated with a massive reduction in populations *G. morsitans morsitans* Westwood and, particularly, *G. pallidipes* Austen in the vicinity of Rekomitjie (Lord *et al.*, 2018). The research station is in a national park with no agricultural interference that could negatively impact tsetse populations, and there has never been any attempt to control tsetse in the area. That being the case, it is reasonable to think that increasing temperature did, indeed, play an important part in mediating declines in tsetse populations. Elsewhere in Zimbabwe, however, other effects were of greater importance than temperature. Thus, there has been, since 1980, rapid expansion of agricultural activity and, particularly in the 1980s and 1990s, vigorous prosecution of tsetse control measures that saw huge reductions in the range of the fly and in the incidence of animal trypanosomiasis (Hargrove, 2003*b*). These, largely anthropogenic, effects could be modified by changes in temperature. In areas, such as the Zambezi Valley, where temperatures have historically been at the hot end of the spectrum for tsetse, further increases could contribute to the kinds of population collapse seen at Rekomitjie. In parts of the middle and highveld areas, however, where winter temperatures have historically been too low to support tsetse populations, increased temperatures could tip the balance in favor of the fly. Similarly, in other parts of Africa, it is important to consider the impact of increasing temperatures on the possibility of, at least, local extinction of tsetse in some parts of the continent and of increased potential for the growth of tsetse populations in other parts which were previously too cold for the flies.

Two published works have estimated extinction probabilities and time to extinction for tsetse populations, by assuming fixed environmental states throughout the life history of the flies. The first (Hargrove, 2005), derived a branching process model for

tsetse populations, with the assumption that male and female offspring are produced with equal probability. This assumption is not generally true (Leak, 1999), although the results obtained in Hargrove (2005) are consistent with published results on tsetse biology. The second publication (Kajunguri *et al.*, 2019) provides a sound mathematical foundation for the results obtained in Hargrove (2005), and assumes a situation where male to female sex ratio can vary anywhere in the open interval $(0, 1)$ and shows how extinction probability depends on the male-female sex ratio in tsetse populations.

In both papers, in order to gauge the importance of various determinants of tsetse population growth, extinction probabilities were calculated for numerous combinations of mortality and fertility rates. There was no explicit modelling of the effect of temperature on vital rates, nor thus on its effect on extinction probabilities. In this paper, we develop a version of the stochastic branching process model presented in Hargrove (2005) and Kajunguri *et al.* (2019) in which all of the biological processes in the tsetse life cycle are explicitly dependent on temperature.

In a model developed to describe the tsetse population dynamics of *G. m. morsitans* on Antelope Island, Lake Kariba, Zimbabwe, it was found that, when temperature was used as an independent variable in the model, adding other climatic factors did not improve the fit of the model to data (Hargrove and Williams, 1998). This suggests that temperature is a key climatic driver of tsetse population dynamics, though we do not discount the importance of other factors such as vegetation cover, humidity and, particularly, access to suitable vertebrate host species. In this study we focus on the impact of temperature on extinction probability, time to extinction, reproduction number and growth rates for tsetse populations in situations where other factors are considered invariant and favorable to the survival of tsetse populations. Even under such circumstances, we show that positive population growth occurs only within quite a narrow band of mean temperature. Sustained temperatures either above or below this band can drive tsetse populations to extinction.

Various researchers have obtained mathematical expressions for the temperature dependence of such functions as daily survival probabilities for young, and mature, adult females, and pupae, and the inter-larval period and pupal duration (Ackley and Hargrove, 2017; Lord *et al.*, 2018; Hargrove and Vale, 2019; Phelps, 1973; Hargrove, 2004, 1999). Using these functions allows us to estimate extinction probabilities, time to extinction and mean of tsetse population size at different levels of fixed temperatures.

It was also assumed in the earlier papers that mortality in adult flies was independent of the age of the fly. Evidence suggests that mortality rates are actually markedly higher in recently emerged adults than in mature flies (Ackley and Hargrove, 2017; Hargrove, 1990; Dransfield *et al.*, 1989; Hargrove, 2001*b*), and that this difference is particularly severe at extremes of high temperatures (Phelps and Clarke, 1974; Ackley and Hargrove, 2017). To capture this difference in mortality rates, we assume higher mortalities for adult females that have not ovulated for the first time, compared with the survival probability of all older flies.

We note at the outset that the temperature relations referred to above generally apply to results from studies on *G. m. morsitans* Westwood. The mode of reproduction is identical in all species of tsetse and it appears that, at temperatures in the region of 25°C, there are only minor variations in the rates at which females produce offspring, and at which the offspring develop (Leak, 1999). Given that all tsetse are poikilotherms, we may also be sure that all rates will be a function of temperature. Nonetheless, the pioneering work of Phelps (Phelps, 1973; Phelps and Clarke, 1974; Phelps and Burrows, 1969*a*,*b*), who measured the detailed effects of temperature on development, and survival, rates of *G. m. morsitans* pupae, have not been carried out in such detail for any other species of tsetse. Similarly, whereas the effects of fly age and environmental temperature on adult mortality have been carefully estimated for this species (Hargrove, 1990; Dransfield *et al.*, 1989), there is little information available on such detailed relationships for most other species.

We may be confident that the mathematical functions presented here will be applicable, in general, to all tsetse, whether savannah, forest or riverine species, and indicate the general trends in extinction probabilities to be expected in these species with changing temperatures. The functions will, however, only produce meaningful and accurate results if appropriate values can be made available for all of the input parameters for individual species. At the moment this is approximately true only for *G. m. morsitans*.

5.3 Materials and methods

We follow the general approach described earlier (Hargrove, 2005; Kajunguri *et al.*, 2019) but the extinction probability is now obtained with fewer mathematical steps, and in a more compact form. We use the solution to obtain numerical results for extinction probabilities, times to extinction and growth rates for tsetse populations

living at various fixed temperatures. We achieve this by using existing functions in the literature relating tsetse fly life cycle parameters to temperature. We modify published versions of the model (Hargrove, 2005; Kajunguri *et al.*, 2019) by separating the adult life stage of tsetse fly into immature and mature classes, allowing us to assess differential impacts of temperature in the two stages.

5.3.1 Tsetse life history

The following provides a brief description of the life cycle; fuller accounts are provided in Hargrove *et al.* (2019). Unlike most other insects, tsetse have a very low birth rate: they do not deposit eggs, instead producing a single larva every $7-12$ days (Hargrove, 1994, 2001*b*). The larva buries itself in the ground and immediately pupates, staying underground as a pupa for between $30-50$ days (Phelps and Burrows, 1969*b*), emerging thereafter as an adult with the linear dimensions of a mature adult, but with poorly developed flight musculature, and low levels of fat reserves. Both sexes of tsetse feed only on blood, and the first 2-3 blood-meals are used to build flight muscle and fat reserves, before the mature female can embark on the production of larvae of her own. All of these processes are temperature dependent. The pupal phase in *G. m. morsitans* increases from 20 days at 32°C to 100 days at 16°C (28 days at 25°C) (Phelps and Burrows, 1969*a*), though few adults emerge at the extremes of temperature. Blood-meals are taken every $2-5$ days, again depending on temperature. The time between adult female emergence and first ovulation is only weakly dependent on temperature and is assumed here to take a constant value of 8 days in the field at Rekomitjie (Hargrove *et al.*, 2019). Thereafter, the period between the production of successive pupae increases from about 7 days at 32°C to 12 days at 20°C (9 days at 25°C) (Hargrove, 1995).

5.3.2 Model

The model development and assumptions are similar to those in Kajunguri *et al.* (2019), differing only in the way that mortality and fertility rates are used in the models. In the earlier works, these rates were simply set at constant values. In the present study we use the fact that the rates are almost all known functions of the temperature experienced by the flies. Accordingly, instead of setting these rates at arbitrary values, we instead allow the environmental temperature to take various values, which then dictate the values of the rates of mortality and fertility to be used in the model. In particular, the following rates are all temperature dependent; pupal duration and inter-larval period, and the daily survival probabilities for female pupae,

adult females that are immature (defined as not having yet ovulated for the first time), and mature adult females. We do not explicitly model the growth of the male part of the population, instead we assume that there is always sufficient numbers of males present to ensure that all females are inseminated.

5.3.3 Model assumptions

In what follows all parameters with subscript T are temperature dependent.

1. An immature adult female tsetse (Ackley and Hargrove, 2017) survives the ν days until it ovulates for the first time with probability $\Omega_T = e^{-\omega_T}$ per day, where ω_T, is the daily mortality rate.

2. A mature female tsetse survives with probability $\lambda_T = e^{-\psi_T}$; per day, where ψ_T, is the daily mortality rate for mature females.

3. Once a female has ovulated for the first time, she deposits a single larva every τ_T days.

4. A deposited larva is female with probability β.

5. The larva burrows rapidly into the soft substrate where it has been deposited and pupates (Lord *et al.*, 2018). The pupa survives with probability $\varphi_T = e^{-\chi_T}$ per day; where χ_T is the daily mortality rate for female pupae.

5. At the end of the pupal period of σ_T days, an immature adult fly emerges from the puparium.

7. The immature female fly is inseminated by a fertile male tsetse after ν days, with probability ϵ.

The probability that a female tsetse produces k surviving female offspring is obtained as:

$$p_k(T) = \frac{\epsilon\Omega_T^{\nu}\lambda_T^{k\tau_T}(1-\lambda_T^{\tau_T})\beta^k\varphi_T^{k\sigma_T}}{(1-\beta\lambda_T^{\tau_T}(\frac{1}{\beta}-\varphi_T^{\sigma_T}))^{k+1}}, k > 0. \tag{5.1}$$

The proof of equation (5.1) can be easily obtained from the proof of equation (7) in the supplementary material of Kajunguri *et al.* (2019). The difference here is simply that the probability is a function of temperature, and we assume also that adult mortality rates are different in young and mature adult stages. We assume that T is time invariant. Our interest is to estimate extinction probabilities for tsetse at fixed temperatures.

Equation (5.1) can be used to derive a function for the extinction using the procedures described in earlier publications (Hargrove, 2005; Kajunguri *et al.*, 2019). A simpler derivation, using the work of Harris (1965), is given here. Suppose $p_k(T)$ follows a geometric series for all T, then:

$$p_k(T) = b_T c_T^{k-1}, \tag{5.2}$$

where $b_T, c_T > 0$.

For equation (5.1) we then have:

$$b_T = \frac{\epsilon \Omega_T^{\nu} \lambda_T^{\tau_T}(1-\lambda_T^{\tau_T})\beta\varphi_T^{\sigma_T}}{(1-\beta\lambda_T^{\tau_T}(\frac{1}{\beta}-\varphi_T^{\sigma_T}))^2}$$

and

$$c_T = \frac{\lambda_T^{\tau_T}\beta\varphi_T^{\sigma_T}}{(1-\beta\lambda_T^{\tau_T}(\frac{1}{\beta}-\varphi_T^{\sigma_T}))}$$

Inserting b_T and c_T into equation (5.2), yields

$$p_k(T) = \frac{\epsilon \Omega_T^{\nu} \lambda_T^{\tau_T}(1-\lambda_T^{\tau_T})\beta\varphi_T^{\sigma_T}}{(1-\beta\lambda_T^{\tau_T}(\frac{1}{\beta}-\varphi_T^{\sigma_T}))^2}(\frac{\lambda_T^{\tau_T}\beta\varphi_T^{\sigma_T}}{(1-\beta\lambda_T^{\tau_T}(\frac{1}{\beta}-\varphi_T^{\sigma_T}))})^{k-1}, k \geq 1 \tag{5.3}$$

It follows (from Harris (1965), page 9) that the generating function $f_T(s)$, for $p_k(T)$ is a fractional linear function, and can be expressed as:

$$f_T(s) = 1 - \frac{b_T}{1-c_T} + \frac{b_T s}{1-c_T s}, 0 \leq s \leq 1. \tag{5.4}$$

5.3.4 Mean of female tsetse population at generation n

Substituting for b_T and c_T in equation (5.4) and taking the first derivative with respect to s, at $s = 1$.

$$\mu_T = f_T'(1) = \frac{\epsilon \Omega_T^{\nu} \lambda_T^{\tau_T}\beta\varphi_T^{\sigma_T}}{(1-\lambda_T^{\tau_T})} \tag{5.5}$$

Equation (5.5) is the reproduction number for a female tsetse population. For a population of tsetse living at temperature T°C, the expected number of female tsetse in the population at generation n is denoted by

$$M(n) = \mu_T^n.$$

5.3.4.1 Remark 1

When $\mu_T > 1$, the branching process is said to be supercritical with extinction probability $q_T < 1$. If $\mu_T < 1$, the branching process is subcritical, which implies, in practice, that each female tsetse produces less than one surviving female offspring on average. Extinction is then certain: i.e., the probability $q_T = 1$. The process is called critical if $\mu_T = 1$, and extinction probability is again certain, $q_T = 1$ (see Axelrod and Kimmel (2015) page 36). In other words, for any tsetse population to avoid inevitable extinction, each female fly must produce on average more than one surviving female offspring in her lifetime.

5.3.5 Extinction probability q_T

The extinction probability is obtained by solving for the fixed points of equation (5.4), that is, we find s such that $f_T(s) = s$. We therefore need to solve:

$$1 - \frac{b_T}{1 - c_T} + \frac{b_T s}{1 - c_T s} = s \tag{5.6}$$

Substituting for b_T and c_T in equation (5.6) and solving for s, the extinction probability $s = q_T$ is the smaller nonnegative root of equation (5.6).

$$q_T = \frac{1 - \lambda_T^{\tau_T}(1 - \beta\varphi_T^{\sigma_T}(1 - \epsilon\Omega_T^{\nu}))}{\beta\lambda_T^{\tau_T}\varphi_T^{\sigma_T}}, \tag{5.7}$$

where $\beta\lambda_T^{\tau_T}\varphi_T^{\sigma_T} \neq 0$.

5.3.5.1 Remark 2

Suppose $\beta\lambda_T^{\tau_T}\varphi_T^{\sigma_T} < 1 - \lambda_T^{\tau_T}(1 - \beta\varphi_T^{\sigma_T}(1 - \epsilon\Omega_T^{\nu}))$, then $\epsilon\Omega_T^{\nu}\lambda_T^{\tau_T}\beta\varphi_T^{\sigma_T} + \lambda_T^{\tau_T} < 1$, which implies that $\mu_T < 1$ (5.5)). Therefore, whenever the denominator of equation (5.7) is less than the numerator, extinction probability $q_T = 1$. Hence, for all biologically meaningful parameter ranges, q_T is always in $[0, 1]$ (See Remark 1). Furthermore, when the initial population consists of a single female fly, the extinction probability is given by equation (5.7). If the initial population is made up of N female flies, the extinction probability is given by $(q_T)^N$ (Kajunguri *et al.*, 2019).

5.3.6 Expected time to extinction for a population of tsetse

An expression for the expected time for a population of female tsetse to become extinct is presented in Hargrove (2005), as:

$$E(K) = \sum_{n=0}^{\infty}(1 - (q_n(T))^N), \tag{5.8}$$

where

$$\phi(q_{n-1}(T)) = \sum_{n=0}^{\infty} p_k(T)q_{n-1}(T) = q_n(T).$$

K is the time to extinction and N is the number of female tsetse flies in the initial population. To estimate the mean time to extinction of a population consisting of N flies, it suffices to calculate $q_n(T)$ iteratively, and raise each value to the power N, to obtain $E(K)$ as given in equation (5.8). Note that, since females produce both male and female offspring, extinction of the female population obviously guarantees the extinction of the whole population.

5.3.7 Tsetse mortality rates as a function of temperature

The relationship between temperature and the instantaneous daily mortality rate of pupae is modelled as a the sum of two exponentials (Fig 5.1) (Hargrove and Vale, 2019).

$$\chi_T = b_1 + b_2 e^{-b_3(T-16)} + b_4 e^{b_5(T-32)} \tag{5.9}$$

Daily mortality rates of young and mature adult female *G. m. morsitans* increase exponentially with temperature (Fig 5.2). The defining equations, (5.10) and (5.11), take the same form, differing only in the parameter values (Table 5.1), due to the higher mortality of young flies, particularly at high temperatures.

$$\omega_T = \frac{e^{-b_6+b_7T}}{100} \tag{5.10}$$

$$\psi_T = \frac{e^{-b_8+b_9T}}{100} \tag{5.11}$$

5.3.8 Development rates as a function of temperature

Pupal duration is modelled as increasing exponentially with decreasing temperature (Hargrove and Vale, 2019; Linden, 1984; Phelps and Burrows, 1969*a*; Hargrove and Ackley, 2015).

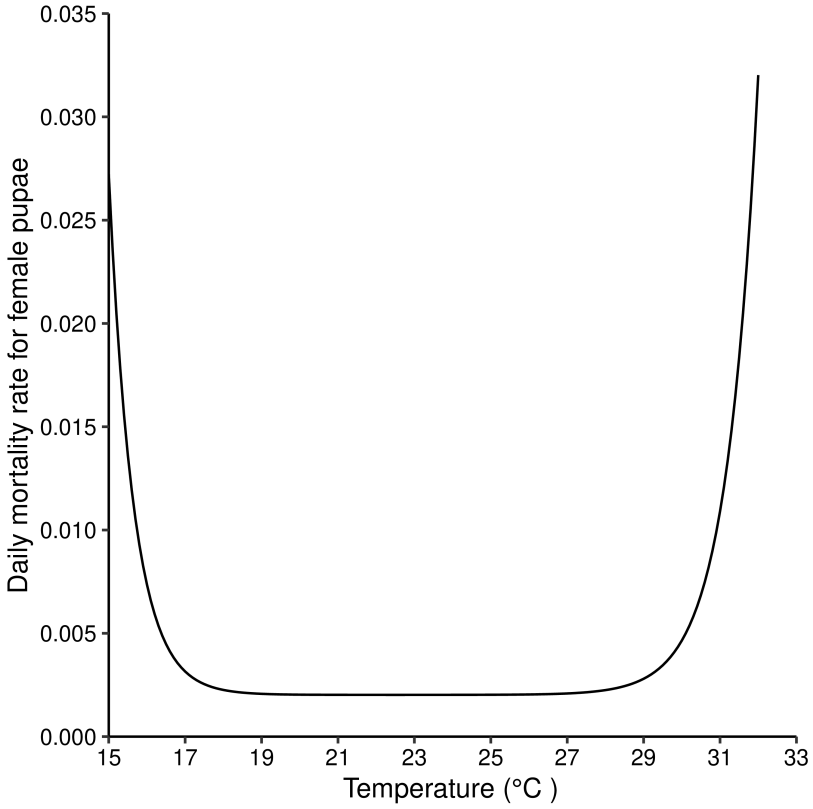

Figure 5.1: Daily mortality rates for female *G. m. morsitans* pupae for temperatures between (15°C-33°C). Equation (5.9) plotted for different values of temperature.

$$\sigma_T = c_1 + c_2 e^{c_3(T-16)} \tag{5.12}$$

The relationship between larviposition rate and temperature was modelled using the results from a mark and release experiment conducted at Rekomitjie on *G. m. morsitans* and *G. pallidipes* (Hargrove, 1994).

$$\tau_T = \frac{1}{d_1 + d_2(T-24)} \tag{5.13}$$

In equations (5.9) – (5.13), b_i, c_i, and d_i are all constants.
Numerical simulations were carried out using RStudio (version 1.1.463) (RStudioTeam, 2016), by incorporating equations (5.9) – (5.13) into equation (5.7) and taking parameter values from the literature as shown in Table 5.1.

We note that it has been demonstrated that computing mean daily fertility in adult female tsetse, using the reciprocal of the interlarval period, under-estimates the true fertility by about 10%: it was also demonstrated that the Antelope Island mark-recapture procedure (Hargrove, 2004) over-estimated mortality among older tsetse

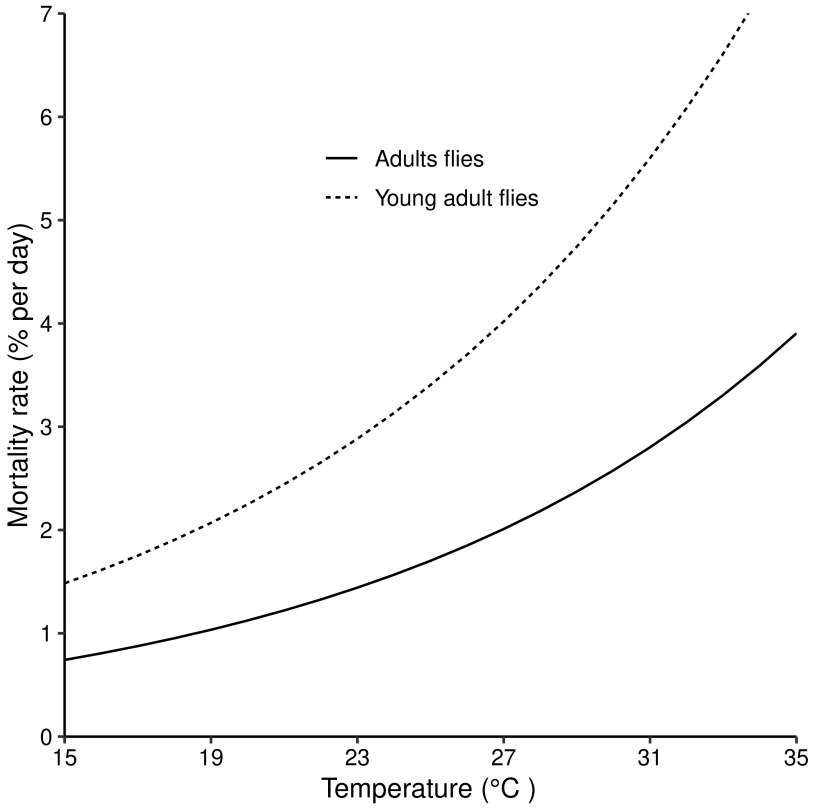

Figure 5.2: Daily mortality rates for young adult and mature adult female *G. m. morsitans* for temperatures ranging from 15°C-35°C.
Equations (5.10) and (5.11) plotted for different temperatures.

(Barclay *et al.*, 2020*a*,*b*). Our development uses the correct procedure for estimating fertility, and we have adjusted the functions relating adult mortality to temperature as suggested in these studies.

Table 5.1: Summary of model parameter values for *G. m. morsitans* and sources: Parameter values are generally sourced from the literature.

Parameter	Description	Value & Source
	Daily female pupal mortality (χ_T)	(Hargrove and Vale, 2019)
b_1		0.00202
b_2		0.00534
b_3	Equation (5.9)	1.552
b_4		0.03
b_5		1.271
	Daily mortality rate for young flies (ω_T)	(Hargrove, 2004)
b_6	Equation (5.10)	-0.85
b_7		0.083
	Daily mortality rate for mature flies (ψ_T)	(Hargrove, 2004)
b_8	Equation (5.11)	-1.60
b_9		0.083
	Pupal duration (σ_T) (days)	(Hargrove, 1994)
c_1		17.94
c_2	Equation (5.12)	82.3
c_3		-0.253
	Inter-larval period (τ_T) (days)	(Hargrove, 2004)
d_1		0.1046
d_2	Equation (5.13)	0.0052
β	Probability deposited pupa is female β	0.5 (Kajunguri *et al.*, 2019)
ν	Time (days) from adult emergence to first ovulation	8.0 (Kajunguri *et al.*, 2019)
ϵ	Probabilty of insemination by a fertile male	1.0 (Kajunguri *et al.*, 2019)

5.4 Results

Given that all tsetse species are poikilotherms, which feed on vertebrate blood meals, and which have identical modes of reproduction, it is reasonable to suppose – until demonstrated otherwise - that the mathematical formulae derived above will be qualitatively the same for all species. It is known, however, that the parameters values will vary between species. In the case of *G. m. morsitans* we have some reasonably good estimates for these required parameter values (Table 5.1). The information is much less complete for all other tsetse species. Strictly speaking, therefore, the results presented below (Figures 5.1 to 5.7) refer only to *G. m. morsitans*. Until such time as parameter estimates are provided for other species we will not know how the results differ in these other species.

5.4.1 Extinction probability as a function of fixed temperatures

Extinction probabilities for *G. m. morsitans* were calculated as a function of fixed temperatures ranging from 15-35°C, for different values of the number of females in the initial population. As expected, sustained extreme temperatures can drive populations to extinction. When the initial population consists of a single female fly, extinction probability did not drop below 0.45 even with optimal temperatures (Fig 5.3). However, when the starting population consists of even 10 female flies, extinction probability drops rapidly to zero as temperatures increase slightly above 17°C.

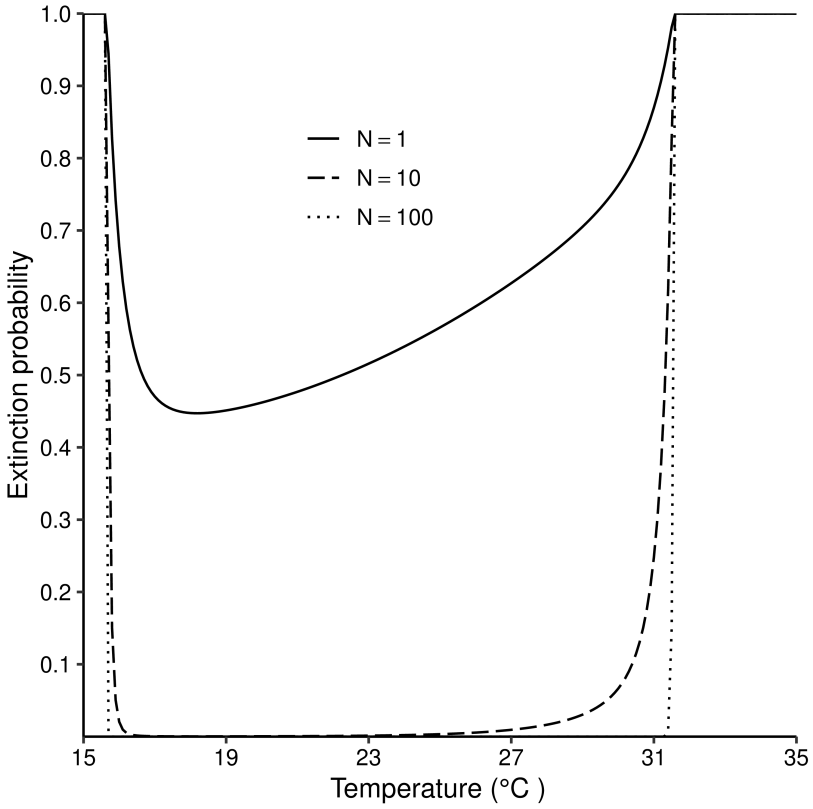

Figure 5.3: Probability of extinction of a population of *G. m. morsitans* as a function of temperature varying between 15°C and 35°C. Equation (5.7) solved for different values of temperature and for different numbers of inseminated adult females in the initial population.

With sufficient female tsetse, say 100, in the initial population, extinction probabilities went rapidly to zero when temperatures exceeded 16°C, and remained at 0 even at temperatures slightly above 31°C. No *G. m. morsitans* population, regardless

of the number of females in the starting population, can escape extinction outside the range of approximately 16°C-32°C (Fig 5.3).

5.4.2 Expected number of females per female *G. m. morsitans* for different levels of fixed temperatures

The reproduction number for a population, i.e., the number of surviving daughters an adult fly is expected to produce in her lifetime, is presented in Figure 5.4 for different levels of fixed temperatures. The reproduction number peaks at 2.8, for temperatures in the neighbourhood of 19°C. It gradually declines as temperatures increase above 21°C, dropping below 1.0 when temperatures exceed about 31°C. However, as temperature decreases below 18°C there is a sharp drop in the reproduction number, which goes below 1.0 at a temperature just below 16°C.

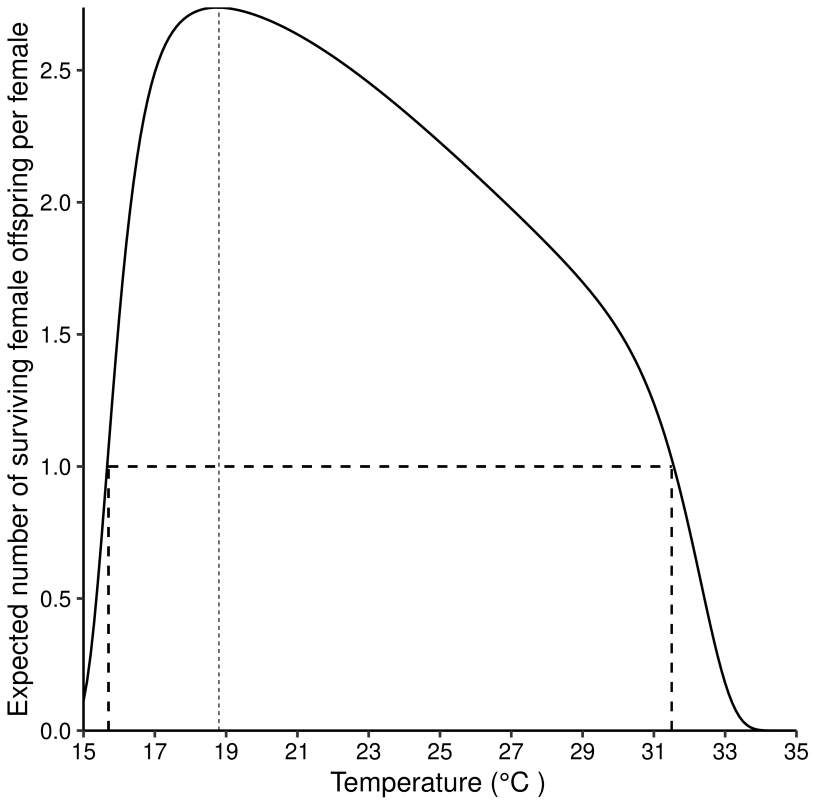

Figure 5.4: Expected number of surviving female offspring per adult female *G. m. morsitans* for different temperatures (15°C-35°C). Equation (5.5) solved for different values of temperature.

5.4.3 Time for the population of female tsetse flies to go extinct at different fixed temperatures

The expected number of generations to extinction varies with temperature and with the size of the starting population. When the simulation for the expected number of generations is performed for 20 generations, it takes 12 generations for a population starting with 2 female flies to go extinct under optimal temperatures of 19-21°C. As temperature increases above 21°C, the number of generations to extinction reduces gradually, but the decrease becomes much more rapid as temperatures approach 31°C When the number of flies in the initial population increases to 10, extinction did not occur in the first 20 generations for temperatures between 16 and 31°C (Fig 5.5).

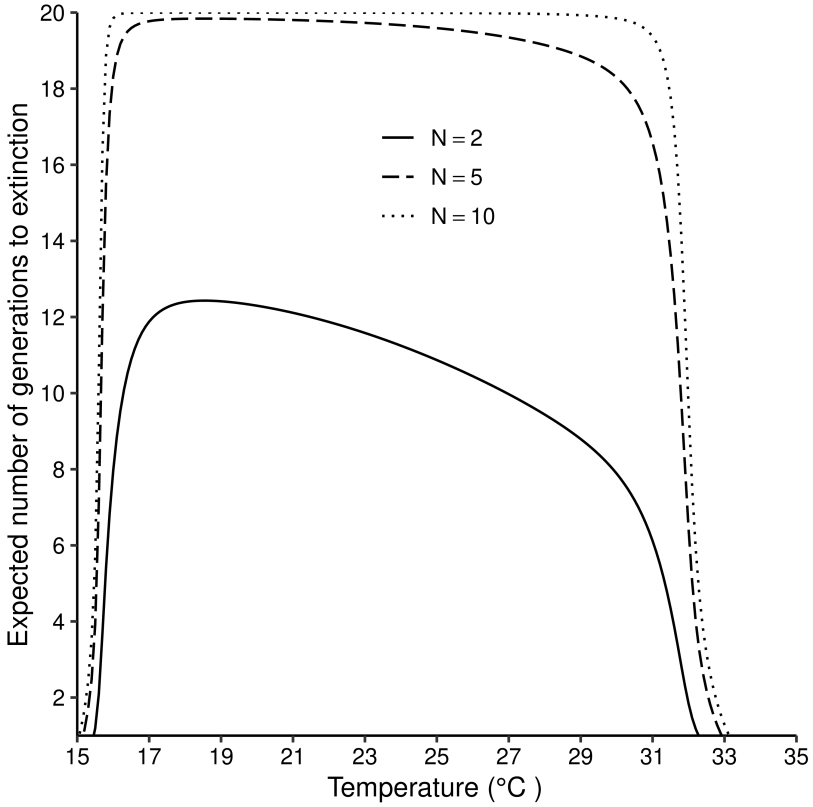

Figure 5.5: Expected number of generation to extinction of a *G. m. morsitans* population for different number of females in the initial population at different temperatures (15°C-35°C). Equation (5.8) is solved iteratively up to $n = 20$.

5.4.4 Growth rates of *G. m. morsitans* populations at different fixed temperatures

Populations of *G. m. morsitans*, which are small enough that we may ignore density-dependent effects, grow exponentially for temperature in the approximate range 16-31°C (Fig 5.6). Notice that, in this figure, growth is plotted as a function of the number of generations completed. The expected number of female tsetse in the population,

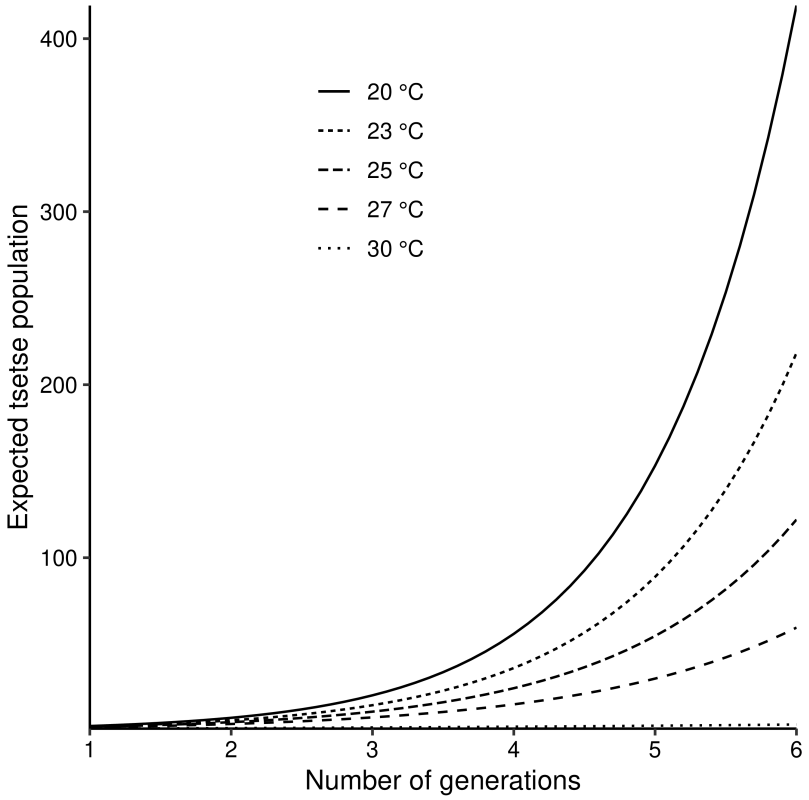

Figure 5.6: Expected growth in the numbers of adult females in a *G. m. morsitans* population at different temperatures (15°C-35°C). The projections are approximately valid for the early stages of growth, before density-dependent processes have noticeable effects.

from the first generation up to the sixth generation, at different levels of temperature, is shown in Figure 5.6. These results are obtained from $M(n) = \mu_T^n$, where n is the number of generations completed, and μ_T is the reproduction number. In order to gauge the growth rate as a function of time it is necessary to adjust for the fact that the generation time increases with decreasing temperature.

We define generation time (γ) as the expected length of time between the instant a female larva is deposited, and the instant that the resulting adult female deposits the first of her own larvae. That is to say, $\gamma = g + \nu + \tau$. The generation time is

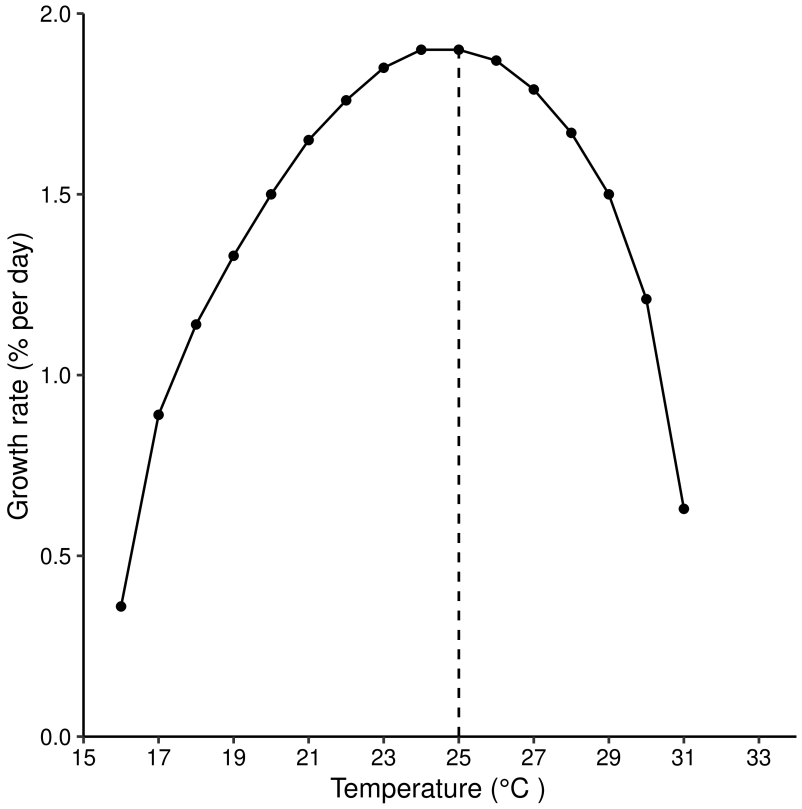

Figure 5.7: Daily growth rate (%) of populations of *G. m. morsitans* living at different constant temperatures (15°C-35°C). After controlling for generation time at different temperature levels.

also temperature dependent – longer during cold seasons and shorter during the hot dry seasons. For example, at 25°C the pupal duration is about 29 days, and the time between adult female emergence and the production of the first larva is about 16 days, giving a generation time of about 45 days. At this constant temperature there would thus be about $365/45 \approx 8$ generation in a year.

To control for generation time, we linearize $M(n)$ by taking the natural logarithm. Furthermore, we divided $\ln(M(n))$ by the generation time for different levels of temperature. We plot $M'(n) = \ln(M(n))/\gamma$ for fixed temperatures from 20°C to 30°C, incrementing by 2°C. The growth rate of tsetse population as a function of fixed temperatures is the slope of $M'(n)$. After controlling for generation time, the growth rate of the population, as a function of calendar time, is seen to take a maximum value of about 2.0% per day at 25°C, falling away increasingly rapidly towards zero as temperatures approach the upper and lower limits of 32°C and 16°C, respectively (Fig 5.7).

5.5 Discussion

The aim of this study was to develop a branching process model for tsetse populations experiencing fixed temperatures of different levels, analogous to laboratory situations where tsetse are kept under regulated temperatures. We estimate extinction probabilities, times to extinction, expected numbers of female offspring per individual female, and growth rates for each scenario. This enables us to determine temperatures that are optimal for population growth rates, and the lower and upper bound temperatures for the survival of *G. m. morsitans* populations.

Our results confirm findings of earlier studies which suggest that temperature is a key driver of tsetse population dynamics (Lord *et al.*, 2018; Nnko *et al.*, 2017; Cecilia *et al.*, 2019). We show that constant temperatures outside the approximate bounds of 16-31°C are fatal for any population of *G. m. morsitans*. These results are also consistent with observations on populations of *G. pallidipes* in the Zambezi Valley of Zimbabwe, where significant reductions in numbers have been attributed to increasing temperatures, particularly at the hottest times of the year (Lord *et al.*, 2018).

As temperatures increase, mortality rates increase for adult female tsetse, and for pupae of both sexes (Hargrove and Ackley, 2015; Ackley and Hargrove, 2017), but larval production rates also increase and pupal durations decline (Hargrove, 2004). In this trade-off, extinction probability initially declines as temperature increase above 15°C (Fig 5.2). In fact even for quite small initial populations the extinction probability falls rapidly to zero for temperatures between 17 and 27°C. Thereafter, however, increases in mortality rates outweigh the increases in birth rates and the extinction probability increases ever more rapidly as temperatures approach 32°C.

When temperatures approach the lower limit of the 16°C–32°C bracket, adult temperature-dependent mortalities decline to low levels, but female tsetse reproduction rates fall drastically as pupal durations increase. In the extreme, when temperatures drop below 16°C, pupal durations are so long that fat reserves are exhausted before the pupa can emerge (Hargrove, 2004). The combination of these factors, if sustained, ensures extinction of *G. m. morsitans* population at these low temperatures (Fig 5.2). Notice that extreme temperatures affect mature adults less than they affect pupae and newly emerged adults. Thus, at a constant mean temperature of 32°C, mature adults suffer a daily mortality of about 2.8%, which still allows positive population growth as long as the mortality among immature stages is not too high. Mortality among young adults is, however, more than double this level at about 6.1% per day: and, crucially, very

few flies survive the pupal stage at 32°C. Similarly, mortality rates among pupae increase exponentially as temperatures decline towards 16°C, whereas loss rates among all adults are smallest at these low temperatures.

Theoretically, for any population to be able to escape extinction, each female adult must produce more than one female offspring, which must themselves survive to reproduce. In epidemiological terms, we then have that the reproduction number, $R_0 > 1$. Figure 5.4 shows that for temperatures below 16°C, female tsetse will not be able to produce enough female flies to sustain the population. If the cold temperature conditions are prolonged, R_0 will drop below 1, resulting ultimately in extinction. Thus, as temperatures approach either hot or cold limits, the number of generations that a population can survive goes rapidly to zero even for large initial population sizes (Fig 5.4).

The reproduction number reached its highest value of 2.8 at 19°C (Fig 5.4). This may, initially, suggest that the growth rate is highest at that temperature. However, when we calculated the actual growth rate after controlling for the length of generation for different temperature values, we found that the population attains its maximum growth rate at 25°C. This result agrees with published values in the literature (Hargrove, 2004), where a different method was used to obtain the same results. It also draws attention to the fact that the reproduction number should be used with caution when comparing two populations with differing lengths of generation.

Our findings are in good agreement with experimental, field and modelling studies of the impact of temperature on different tsetse species (Lord *et al.*, 2018; Nnko *et al.*, 2017; Kleynhans and Terblanche, 2011; Edney and Barrass, 1962; Pagabeleguem *et al.*, 2016), For instance, in Pagabeleguem *et al.* (2016) an experiment was conducted on three different strains of *G. palpalis gambiensis*, in a bid to determine critical temperature limits for tsetse survival and their resilience to extreme temperatures. For the three strains, a temperature of about 32°C was reported as the upper limit of survival. Our results showed, similarly, that, if the number of female flies in the population are high enough, tsetse population may escape extinction at temperatures slightly above 31°C but will go extinct at higher temperatures. The experiment also reached the conclusion that temperatures of about 24°C are optimal for rearing this species, in good agreement with our modelling results.

As global average temperature continues to rise, Africa has also experienced increasingly high temperatures over the past decades (Collins, 2011). For instance, in

the Zambezi Valley of Zimbabwe the monthly mean temperature has increased by 2°C during the hot dry season (Lord *et al.*, 2018). Our results indicate that if the average temperature continues to rise in the Zambezi Valley and other parts of Africa, tsetse populations will go extinct in the hotter parts of the continent, especially in places with similar climate and environmental profile to Zimbabwe. Consequently, future plans for tsetse and trypanosomiasis control and elimination must consider the impact of climate change on tsetse population dynamics in different parts of Africa.

More detailed work, beyond the scope of this study, would be required to produce predictions about how growth rates of particular populations would be affected by various projected changes in temperature profiles. Moreover, deciding on the likelihood of various predicted climate change scenarios is again beyond the scope of this study. We are currently working on such problems and, in particular, the question of how to estimate growth rates of populations subjected to the real-life situations where temperatures cycle daily and annually

5.6 Limitations of the study

Extinction probabilities for tsetse populations have not previously been estimated as a function of temperature. Our modelling framework took into consideration the fact that, as poikilotherms, tsetse mortalities, and rates of larval deposition and pupal development are all temperature dependent. However, the present study did not consider field situations where temperatures vary continuously with time. A modelling framework which will consider this more realistic situation is under construction.

In this study, we considered closed tsetse populations, where there was no in-or-out migration. Estimation of extinction probabilities for populations that are open to migration are markedly more complex and were beyond the scope of the present study. We do note, however, that a preliminary study found that if tsetse populations are in patches, which can compensate for each other, then extinction probabilities are lower than in closed population models (Peck, 2012). Further work in this area is called for.

We caution that the modelling here is restricted to situations where population numbers lie below the level at which density-dependent effects play a significant role. When numbers are larger, however, suppose pupal and/or adult mortality increases with density. Then the temperature-dependent mortalities quoted here provide a lower limit of the true mortality at that time, for any given temperature. Similarly, if

density-dependence results in a decrease in the birth rate, then the birth rates quoted here provide an upper bound to the true birth rate. For such a population, it then follows that the growth rate at any temperature will be lower than calculated here. Moreover, as temperatures increase, or decrease, towards the upper or lower bounds, respectively, for positive population growth, the population will decline rapidly towards levels where the density-dependent effects fall away. At that point the further dynamics of population growth would be subject to the vital rates used in this study.

Temperature is, of course, only one of many factors that decide whether or not tsetse will occur at all in an area and, if they do, the rate at which their populations may be expected to grow. Other climatic, and vegetation, factors, such as rainfall and normalized difference vegetation index (NDVI), have been shown to be good indicators of the presence or absence of tsetse (Rogers and Robinson, 2004). Tsetse will not occur, however, in areas where there are no hosts – regardless of the climatic suitability for the flies (Lord *et al.*, 2017). Similarly, tsetse populations often disappear from areas that are climatically suitable, through the effects of human activities (Bourn *et al.*, 2001). Given these levels of complexity, the detailed analysis required to judge the circumstances under which individual, real, tsetse populations would go extinct, is beyond the scope of this paper. What we have done is to provide the theoretical framework for workers, with access to the climatic, biological, and other data, to be able to predict the effects of temperature changes, when viewed in the context of these other variables.

Finally we repeat the caution that the quantitative results shown in Figures 5.1-5.7 apply to *G. m. morsitans*. Further laboratory and field work would be required in order to generate many of the input parameters required for other species.

Chapter 6

Insect demography: does it matter whether we count babies or mummies?

6.1 Abstract

As insect populations decline, due to climate change and other environmental disruptions, there has been an increased interest in understanding extinction probabilities. Generally, the life cycle of insects occurs in well-defined stages: when counting insects, questions naturally arise about which stage to count and the appropriate point to start counting. Using tsetse (vectors of the trypanosomiases) as a case study, we develop a model that works for different counting points in the life cycle of a fly. Previous branching process models for tsetse populations only explicitly represent newly emerged adult female tsetse, and use that subpopulation to keep track of population growth/decline. Here we directly model other life stages. We analyse reproductive numbers and extinction probabilities, and show that several previous models used for estimating extinction probabilities for tsetse populations are special cases of the current model. We establish that the reproduction number is the same for different counting points, but the outcomes of simulating dynamics from one pupa or one larvipositing female in terms of eventual extinction probability are quite different. We demonstrate, and provide a biological explanation for, a simple relationship between extinction probabilities for the different counting points, based on the probability of recruitment between stages. These results offer insights into insect population dynamics and provide tools that will help with more detailed models of insect populations. Demographic studies of insects should be clear about life stages and counting points.

6.2 Introduction

Insects play key ecological roles, both positive and negative, for the health of plants and animals, including humans, and for the environment in general (Ollerton *et al.*, 2011; Öckinger and Smith, 2007). Many are important vectors of plant and animal diseases, often of public health importance (Tobias, 2016; Wamwiri and Changasi, 2016; Beier, 1998), whereas others are beneficial in, for example, pollination, and some serve as source of protein for massive numbers of species of animals including humans (Ramos-Elorduy *et al.*, 1997). Biologists are accordingly interested in insect population persistence for various reasons. Conservationists are concerned about the ecological implications of extinction of insect populations, while vector biologists or epidemiologists are interested in controlling or eliminating insect vectors of disease (Burt, 2014; Shaw *et al.*, 2013; Hocking *et al.*, 1963).

There is evidence of steep declines in insect populations in different parts of the world (Conrad *et al.*, 2002; Potts *et al.*, 2010; Ilyinykh, 2011; van Swaay *et al.*, 2013; Lister and Garcia, 2018). Hallmann *et al.* (2017) reported a decline of 75% in the biomass of flying insects over a 27-year period in 63 protected areas of Germany. Similar findings of major decline have been reported across the globe (Habel *et al.*, 2015; Pelton *et al.*, 2019). For instance, there was a decline of 50% in the population abundance of European grassland butterflies between 1990 and 2011 (van Swaay *et al.*, 2013), and it has been reported that tsetse populations have been declining in the Zambezi Valley of Zimbabwe (Lord *et al.*, 2018). If the magnitude of the declines is as serious as reported, we may soon witness extinction of huge numbers of insect species.

Insects have limited thermo-regulatory capacity, making them particularly vulnerable to changing temperature regimes – in particular, to the effects of global climate change. There is therefore a growing interest in how increases in global temperature will impact insect populations. Questions about extinction of insect populations are now being asked more frequently (Nilsson *et al.*, 2017). Accordingly, there is a need to continue to improve the accuracy of our prediction of the probability of extinction events in insects – and indeed other animals and plants.

The life history of holometabolous insects occurs in well-defined stages. The question thus arises as to how the developmental stage of counted individuals affects demographic conclusions – for example, the probability that a population will go extinct. We investigate this problem, using populations of tsetse (*Glossina* spp.) as an example. Tsetse are vectors of trypanosomiases (Wamwiri and Changasi, 2016; Kioy *et al.*, 2004); a group of deadly diseases called African sleeping sickness in humans

and nagana in livestock (Kioy *et al.*, 2004). The life cycle of the fly involves five distinct stages; namely, egg, larva, pupa, newly emerged adult, and mature adult (Ackley and Hargrove, 2017). We ask: how would counting different insect life stages affect our calculation of the probability that an insect population will persist under various circumstances?

Several researchers have developed mathematical models to explore different phenomena in insect population dynamics, but are generally not clear about which developmental stage(s) are being counted (Ylioja *et al.*, 1999; Artzrouni and Gouteux, 2003; Hargrove, 2005; Adams *et al.*, 2005; Barclay and Vreysen, 2011; Peck and Bouyer, 2012; Lin *et al.*, 2015; Kajunguri *et al.*, 2019). As far as we are aware, no published work has explicitly considered the implication of counting insects at different stages for the estimation of extinction probabilities for insect populations. Hargrove (2005) developed and analysed a branching process model to derive expressions for extinction probabilities, times to extinction, reproduction number and variance for closed populations of tsetse. The results reported were consistent with published vital rates for tsetse (Hargrove, 1988), and showed that small increases in mortality rates could drive any population of tsetse to extinction. Kajunguri *et al.* (2019) added proofs and improved on some of the assumptions in Hargrove (2005). Are and Hargrove (2020*a*) extended this work to provide estimates of extinction probabilities, growth rates, reproduction number and times to extinction as a function of ambient temperature.

In the above studies, the modelling framework was built on the assumption that the pioneer population starts with one or more newly emerged adult female tsetse. In the current study, by contrast, we generalise the approach – allowing counts of juveniles, emergent females or mature females. We establish a relationship between the extinction probabilities for tsetse populations where the initial population starts at different life stages. We discuss the implications of these results to tsetse population persistence, particularly in the context of tsetse regional control/eradication exercises.

6.2.1 Brief description of tsetse life cycle

Female tsetse typically mates once in their life-time: the sperm transferred by a male during mating is sufficient for the female to fertilize all subsequent eggs throughout her life. A female fly produces, typically every 9-11 days, a single larva, which may weigh as much or even more than she does herself. The larva burrows into the soil and pupates within minutes. The pupal period lasts 30-50 days (Phelps and Burrows, 1969*b*), depending on soil temperature. After the pupal period, an immature adult emerges. It takes 7-9 days, depending on temperature, for the newly emerged adults

to attain full maturation. During this period females are typically inseminated by a male tsetse, and virtually all will have ovulated by the age of 10 days (Hargrove, 2012). The fully developed adult typically larviposits every 9-11 days afterwards (Hargrove *et al.*, 2019).

6.3 Mathematical Model

Our model of tsetse demography is based on two flow diagrams (Figures 6.1 and 6.2). The first flow diagram illustrates the biological processes associated with the tsetse. The state variables and the parameters are described below.

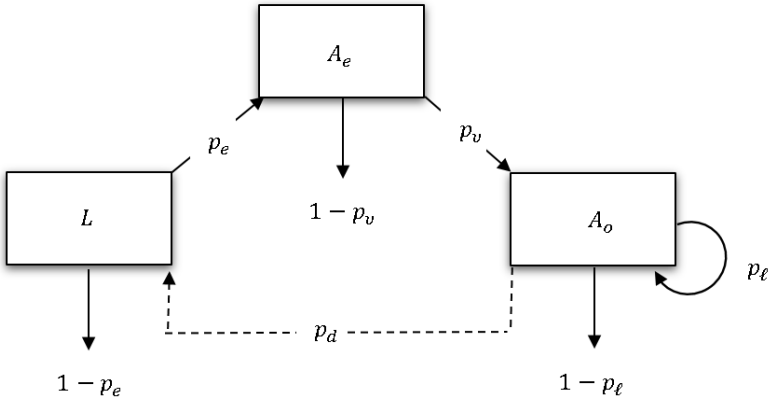

Figure 6.1: A schematic diagram for the tsetse life cycle. The directed arrows pointing to, and away from the boxes, indicate various biological processes in the life cycle of a female tsetse. These include larviposition, emergence as young adult, and development from young adults to mature adult. The lines pointing downward show losses at various life stages.

- L: Newly deposited larvae
- A_e: Emergent adults
- A_o: Adults in the larviposition loop
- p_ℓ: Probability of completing a larviposition loop
- p_d: Probability of depositing a live female larva
- p_e: Probability a deposited female larva emerges as an adult
- p_ν: Probability a newly emerged adult reaches the larviposition loop

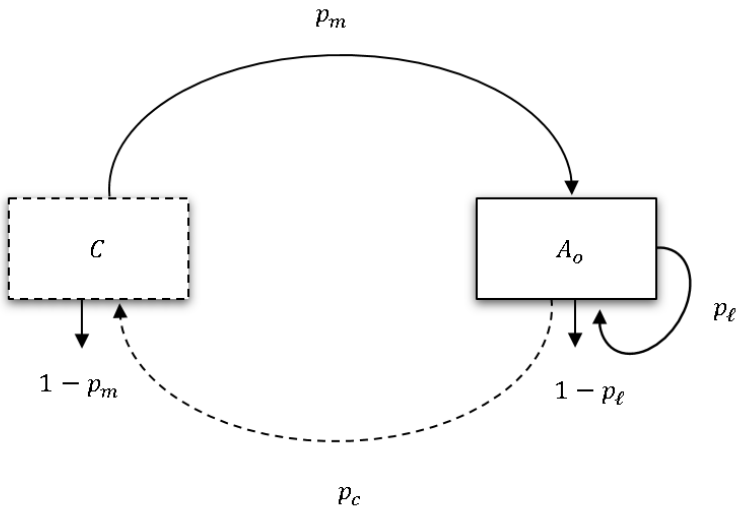

Figure 6.2: Schematic diagram for counting tsetse. The dashed box indicates that the stage at which the individuals are counted can vary. The dashed line from A_o to C, shows the process of producing offspring that are counted, while the solid line from C to A_o indicates the process of being counted, and developing to maturity (reaching larviposition loop).

The second flow diagram presents the counting system. The C inside the dashed box indicates the point where tsetse are counted, while A_o is as described above. The counting point can vary: one may choose to count tsetse at the juvenile stages, or at the mature stages e.g. larvipositing females. The framework we present here allows us to calculate the extinction probability and the basic reproduction number for tsetse population, for all possible counting stages.

The list below shows variables and parameters description.

- A_o: Adults entering larviposition loop
- C: The census point
- p_m: Probability of surviving from the time of being counted to becoming mature (entering the loop)
- p_c: Probability of surviving from loop completion to producing something that is counted
- p_r: Probability of recruitment ($p_r = p_m p_c$)

6.3.0.1 Model formulation

To make our mathematical derivations simple and compact, we use the *odds* associated with the probability that a female completes a larviposition loop and the probability

that it produces a female offspring before dying, to derive the offspring distribution function for tsetse populations.

An individual at the census point:

- reaches the loop with probability p_m
- either goes around the loop producing offspring that will be counted, or else dies in the process.

The probability p_b of producing before dying has odds of:

$$\sigma_b = \frac{p_b}{1-p_b} = \frac{p_\ell p_c}{1-p_\ell} = \sigma_\ell p_c$$

.

The total number of censused individuals produced by a censused individual is:

- 0, if it does not reach the loop (probability $1-p_m$) and
- k, which could also be 0, if it reaches the loop and then fails after k successes, with probability $p_m p_b^k (1-p_b)$.

The associated generating function is:

$$G(s) = 1 - p_m + p_m(1-p_b)\sum_k p_b^k s^k = 1 - p_m + \frac{p_m(1-p_b)}{1-p_b s}.$$

We get $\mathcal{R}$, the reproduction number, by calculating $G'(1)$ (Bartlett, 1949), where

$$G'(s) = \frac{p_m p_b (1-p_b)}{(1-p_b s)^2}.$$

Hence,

$$\mathcal{R} = G'(1) = \tfrac{p_m p_b}{(1-p_b)} = p_m \sigma_b = p_m p_c \sigma_\ell = p_r \sigma_\ell$$

Depending on the counting point, p_m and p_c will vary, but their product will remain the same for all counting points. Therefore, $\mathcal{R} = p_d p_e p_\nu \sigma_\ell$. This implies that regardless of the life stage at which we count the flies, the expected number of offspring produced by an individual in that stage, which will be counted at the same stage, is the same for all counting points.

We get the probability y that a tsetse population, starting with a single individual at a given count point, goes extinct, by solving $G(y) = y$ (Bartlett, 1949). We can

simplify things by solving $G(1-z) = 1-z$, where z is the probability of not going extinct, and then factoring out a z. This gives:

$$z = p_m(1 - 1/\mathcal{R}).$$

By factoring out the z, we are assuming that the process is supercritical, that is $\mathcal{R} > 1$. When $\mathcal{R} \leq 1$, the population will eventually go extinct with probability 1.

Therefore, the probability of extinction for tsetse populations at any counting point is:

$$y = 1 - p_m(1 - 1/\mathcal{R}). \tag{6.1}$$

When there is more than one individual in the pioneer population, we calculate the extinction probability by assuming that density dependence in negligible, and that overall extinction would therefore result from the independent extinction of the line starting from each individual. Thus, the extinction probability is:

$$y_j = (1 - p_m(1 - 1/\mathcal{R}))^j,$$

where j is the number of individuals in the given stage. We can derive extinction probabilities for tsetse populations at the individual counting points by making simple substitutions for the probabilities of recruitment between stages in p_m in equation (6.1), as appropriate.

6.4 Counting tsetse at different life stages

When we change the counting stages by moving the dashed box (Figure 6.2) closer to the ovulation loop, $\mathcal{R}$ stays the same but p_m gets larger until it reaches 1 when the dashed box gets to the ovulation loop. We can thus calculate extinction probabilities for each of our the three counting points. We first ask what happens if we start from a single newly deposited female larva. The larva reaches the larviposition loop (emerges and then matures) with probability $p_m = p_e p_\nu$, completes a larvipositing loop with *odds* σ_ℓ, and produces surviving female larvae with probability $p_c = p_d$. When we make appropriate substitutions in y, the extinction probability for a population of tsetse with a newly deposited larva in the initial population is:

$$y_l = \frac{1 - p_\ell(1 - p_d(1 - p_e p_\nu))}{p_\ell p_d}.$$

This can be written more compactly in terms of $\mathcal{R}$ as:

$$y_l = 1 - p_e p_\nu (1 - 1/\mathcal{R}) \tag{6.2}$$

In similar fashion, we can obtain the extinction probability y_e for a tsetse population starting with a single newly emerged adult fly, by substituting $p_m = p_\nu$ in y above. We find:

$$y_e = \frac{1 - p_\ell(1 - p_d p_e(1 - p_\nu))}{p_d p_e p_\ell}, p_d p_e p_\ell \neq 0.$$

This can be rewritten in terms of $\mathcal{R}$ as:

$$y_e = 1 - p_\nu(1 - 1/\mathcal{R}). \tag{6.3}$$

Furthermore, when larvipositing females are counted, p_m will be equal to 1. The extinction probability y_o for a population of tsetse starting with a single larvipositing female tsetse in the initial population is, therefore:

$$y_o = \frac{1 - p_\ell}{p_d p_e p_\nu p_\ell}.$$

This can be expressed in terms of $\mathcal{R}$ as:

$$y_o = 1/\mathcal{R} \tag{6.4}$$

It is easily verifiable that whenever $\mathcal{R} > 1$ the following inequality holds:

$$y_o \leq y_e \leq y_l \tag{6.5}$$

6.4.1 Remarks

- In our analysis so far, we have focused on populations starting with a single individual in the initial population. In the general case, assuming extinction probabilities for the population starting from each individual for each counting points are independent, the extinction probability for a population starting with N_l larvae, N_e newly emerged adult females and N_o larvipositing adult females, is just the product of the individual extinction probabilities.

$$\tilde{y_c} = y_l^{N_l} y_e^{N_e} y_o^{N_o}.$$

- The current analysis focuses strictly on female tsetse populations. We can account for this by expressing p_d (probability of depositing a live female larva) as: $p_d = \delta\beta$, where δ is the probability that a deposited larva is alive, and β the probability that a deposited larva is female. These two parameters (δ and β) will allow us to capture both male-to-female sex ratio in the population, and the abortion rates in tsetse population. If we set $\beta = 0.5$ and $\delta = 1$, the current model corresponds to the model presented in Hargrove (2005).

6.4.2 Example 1

We provide an example to show that previous estimates for extinction probabilities for tsetse populations are special cases of the current framework. It can be shown easily that the models presented in Hargrove (2005), Kajunguri *et al.* (2019), Are and Hargrove (2020*a*) correspond to the scenario presented above-counting newly emerged adults. In Are and Hargrove (2020*a*), the following parameters and descriptions were used to derive a probability distribution function for female tsetse population:

- ϵ, the probability that a female is inseminated by a fertile male
- Ω^{ν}, the probability that a newly emerged adult survives until first larviposition
- λ^{τ}, the probability that an adult survives until it deposits a pupa (completes a cycle)
- β, the probability that a deposited pupa is female
- ϕ^{σ} the probability that a deposited pupa emerges

Here, the exponents are associated with daily probabilities and represent the number of days an insect needs to survive a given stage.

The probability that a female tsetse produces exactly k surviving daughters in her lifetime is p_k, given as:

$$p_k = \frac{\epsilon\Omega^{\nu}\lambda^{k\tau}(1-\lambda^{\tau})\beta^k\phi^{k\sigma}}{(1-\beta\lambda^{\tau}(\frac{1}{\beta}-\phi^{\sigma}))^{k+1}}, k > 0 \tag{6.6}$$

Setting $p_{\nu} = \epsilon\Omega^{\nu}$, $p_{\ell} = \lambda^{\tau}$, $p_d = \beta$ and $p_e = \phi^{\sigma}$ in $G(s)$ above, shows that the models used in the works cited above, are special cases of the current model.

6.5 Numerical Results

We adopt the parameter descriptions presented in example 1, and simulate the model results using RStudio (version 1.1.463) (RStudioTeam, 2016). We assume that key parameters are all temperature dependent and their relationship with temperature follows from Are and Hargrove (2020*a*)

Figure 6.3 shows extinction probabilities for different counting points as a function of different levels of fixed temperatures, which the flies are experiencing. Extinction probabilities for the three counting points are plotted for the same range of temperature (15 °C-33°C) and different initial population sizes. For temperatures within the

survival limit for tsetse populations (16°C-31°C) (Are and Hargrove, 2020*a*), extinction probabilities are highest for populations of tsetse starting with a single larva. Extinction probabilities are least when we start with female adults in the larvipositing loop. Extinction probability is 1 for all counting points for all constant temperatures outside the range (16°C-31°C)(Fig 6.3 A). When the starting population size is larger, say 100, extinction probabilities approach 0 for temperatures in the range 16 - 31°C for all counting points (Fig 6.3B).

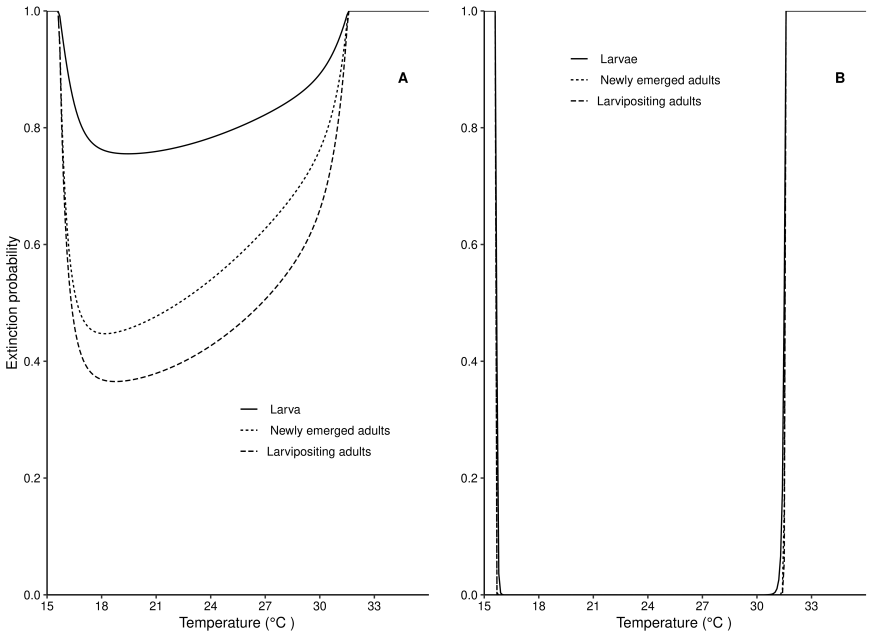

Figure 6.3: Extinction probability as a function of temperature (15°C-33°C) for different counting points. (A) When pioneer populations consist of 1 individual (larva, newly emerged adult, or larvipositing adult). (B) When pioneer population consist of 100 individuals.

We assume a fixed temperature of 24°C, and simulate extinction probabilities as a function of the daily mortality rates for female pupae (for the three counting points) starting with different initial population sizes. Extinction probabilities increase, and approach 1, as the daily mortality rates for female pupae increases. This is true for the three counting points. When pupal mortality rate is $\geq$ 3.1% per day, the extinction probability is 1 for the three counting points (Fig 6.4B).

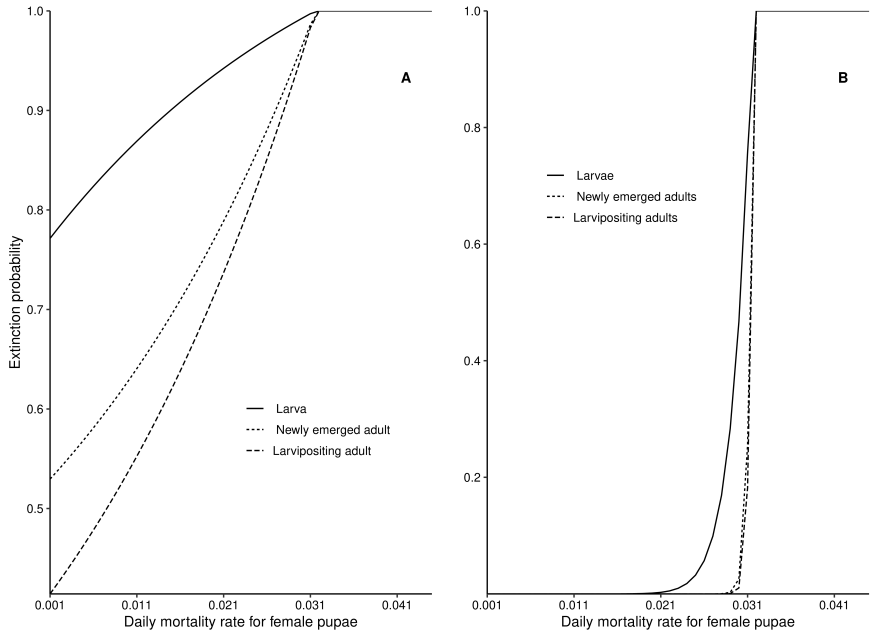

Figure 6.4: Extinction probability as a function of daily mortality rates for female pupae, at 24°C, for different count points. (A) Extinction probabilities for 1 pioneer individual (B) Extinction probabilities for 100 pioneer individuals.

We present extinction probabilities as a function of the daily mortality rates for newly emerged adults. Extinction probabilities increase, for the three counting points, as the daily mortality rate for newly emerged adults increase. When the size of the initial population is increased to 100, for all counting points, extinction probability is 0 for daily mortality rates below 12% per day. Extinction probability rapidly goes to 1, for all counting points, as daily mortality rate for newly emerged adults is $\geq$ 15.1% per day (Fig 6.5).

Extinction probabilities are plotted as a function of daily mortality rate for larvipositing adult females, for different counting points. There is a marked difference in extinction probabilities when the starting populations consist of a single larva, newly emerged adult or larvipositing adult, respectively. However, when the initial population is increased to 100, extinction probabilities go to 1, rapidly, for all counting points, when the daily mortality rate $\geq$ 3% per day for larvipositing adults (Fig 6.6).

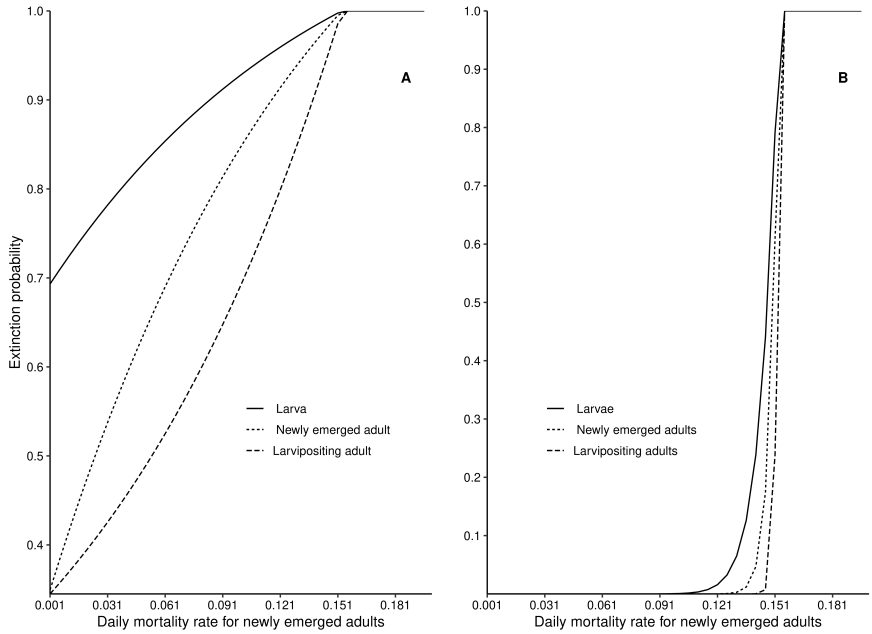

Figure 6.5: Extinction probability as a function of daily mortality rates for newly emerged adults at 24°C, for different count points. (A) Each line represents extinction probabilities for a single larva, or newly emerged adult or larvipositing adult, respectively, in the initial populations (B) When pioneer populations consist of 100 larvae, or newly emerged adults, or larval positing adults, respectively.

When we increase the starting population to 500, for each counting points, extinction probabilities stay at 0 for all values of the daily mortality rate for adult females which are less than 3% per day, daily mortality rates for newly emerged adults that are less than 15.1% per-day and daily pupal mortality rates that are less than 3.1% per-day. Moreover, when the daily mortality rate for larvipositing female reaches 3.1% per day, or daily mortality rate for newly emerged adults exceeds 15.1% per-day or daily mortality rate for female pupae exceeds 3.1% per-day, extinction probability rapidly goes to 1, for each of the counting points respectively.

6.5.1 Extinction probabilities for different levels of abortion rates

Our model suggest that abortion rates $(1 - \delta)$, will only be an important factor in the extinction of a tsetse population if the rates approach or surpass 50% (Fig 6.7). Field studies suggest that abortion rates in normal, healthy populations of tsetse are generally low (Madubunyi, 1975, 1978; Okiwelu, 1977a,b; Turner and Snow, 1984; Hargrove, 1999). Hargrove (1999) showed that abortion rates did increase markedly at the hottest time of the year in the Zambezi Valley of Zimbabwe but, as temperatures rise, there are also increase in the pupal and adult mortality. Our modelling suggests

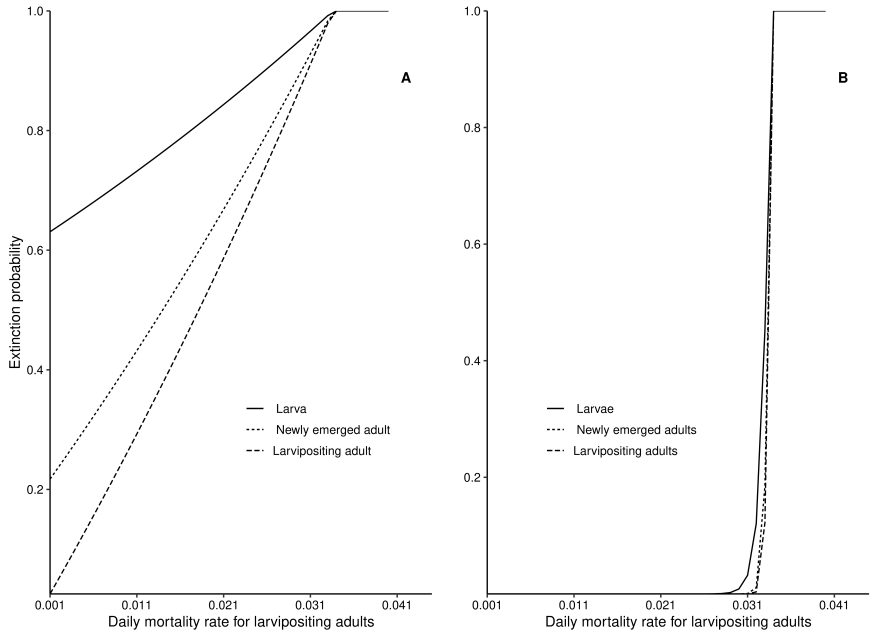

Figure 6.6: Extinction probability as a function of temperature and daily mortality rates for larvipositing female adults at 24°C, for different count points. (A) Each line represents extinction probabilities for a single larva, or newly emerged adult or larvipositing adult, respectively, in the initial population. (B) When pioneer populations consist of 100 larvae, or newly emerged adults, or larvipositing adults, respectively.

that these increases will have more substantial effects on tsetse population growth rate than the changes in the abortion rate.

6.6 Discussion

The life cycles of holometabolous insects, such as tsetse, can be divided into five distinct stages, egg, larva, pupa, immature adult, mature (larvipositing) adult– each with distinct physiological features, and with differing responses to various environmental factors. In tsetse, for example, the most vulnerable stage is newly emerged adults, which also appear to be particularly susceptible to high temperatures (Ackley and Hargrove, 2017): Tsetse are unusual in that survival probability is high in the egg and larval stages, which are retained in the mother's uterus (Hargrove, 1999). In this study, we investigate whether counting different stages influences our estimates of insect population persistence and basic reproduction number. We used a simple, unified model to analyse extinction probabilities when starting from different life stages, and confirmed that we can calculate consistent reproductive numbers for each counting point.

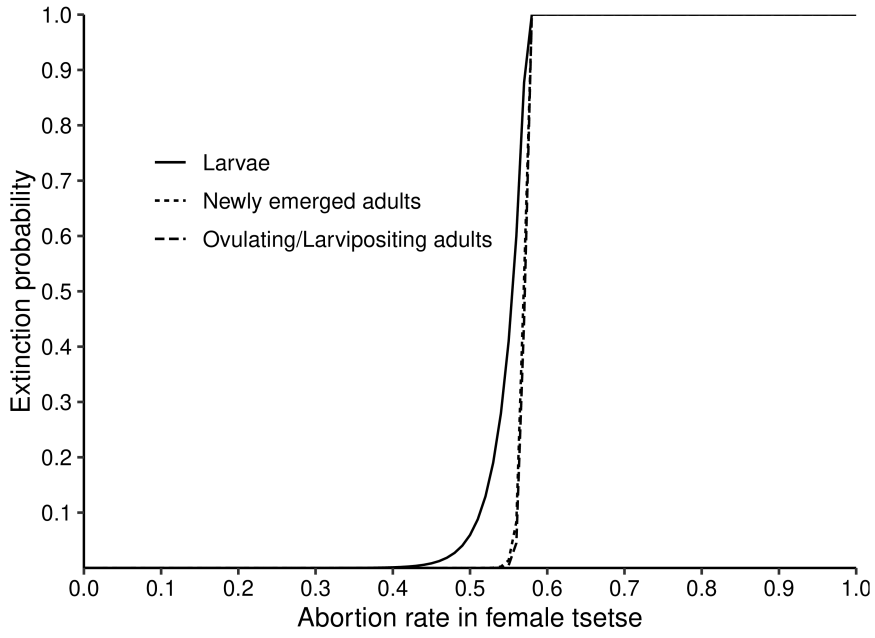

Figure 6.7: Extinction probability as a function of abortion rate at 24°C When pioneer populations consist of 100 larvae, or newly emerged adults, or larvipositing adults, respectively.

We demonstrated that our estimate of the basic reproduction number was independent of our choice of the stage we counted. It does not matter whether we start with larvae, newly emerged adults or larvipositing adults, the average number of offspring an individual female is expected to produce remains the same. On the other hand, the estimated extinction probability is different for each counting stages. If we assume that the initial population consists of a single larva, extinction probability is higher than when the initial population consists of individuals that are either newly emerged or larvipositing adults. As indicated above, each stage of the tsetse life cycle typically experiences different mortalities (Hargrove, 2005). The newly emerged adults, for instance, have higher mortality rates than the larvipositing adults (Hargrove and Vale, 2019). Even though the basic reproduction number does not depend on the stage that we count, a population which starts with larvipositing adults will have a higher chance of escaping extinction than a population which consists of larvae or newly emerged adults in its initial population. Notice, however, that this effect is only well marked when the size of the initial population is low. When the number of larvae, or newly emerged adults in the initial population is large, say > 500, then it does not matter which stage we chose to count, the probability of extinction remains the same for all stages.

We calculated extinction probabilities as a function of fixed temperatures between 15°C and 35 °C for different counting points. The results agree with previous findings

on temperature survival limits for tsetse population (Edney and Barrass, 1962; Kleynhans and Terblanche, 2011; Pagabeleguem *et al.*, 2016; Are and Hargrove, 2020*a*). No tsetse population, regardless of the counting stage, can survive temperatures $<$ 16°C or $>$ 31°C, if exposed to these temperatures for a long period. When the initial population consists of a single individual, extinction probability did not drop below 0.3, regardless of the counting stage, even at optimal temperatures. When the initial population consists of a large population (>100 for each counting stage), extinction probability is zero for all temperatures within the limits 16 °C-31 °C, for all counting points (Fig 6.3). The larger the size of the initial population the greater the chance of survival of tsetse populations. Tsetse populations can escape extinction at temperatures close to the lower and upper survival bounds, provided the initial population size is large (Figs 6.3-6.6).

We set the temperature to 24 °C, which is the ideal temperature for optimal growth in tsetse population (Pagabeleguem *et al.*, 2016; Are and Hargrove, 2020*a*), and calculated extinction probabilities at different levels of pupal mortality. For a population consisting of a single larva, extinction probability is high, at 0.78, even at low daily mortality rates for female pupae (0.1% per-day). A population starting with a single larva is likely to go extinct even if the pupa is kept at optimal temperatures. A population starting with a single larvipositing adult has the highest chance of escaping extinction compared to other counting stages. As the daily mortality rates among female pupae increases to 3.1% per day, extinction probability goes to 1 in all cases. Moreover, when the size of the initial population is increased to 100 for each counting stage, the population will not go extinct for daily mortality rates for adult pupae that do not exceed 2.1% per-day. At 25 °C, no tsetse population can survive if subject to a pupal daily mortality rate of 3.1% (Hargrove and Vale, 2019).

We obtained extinction probabilities as a function of daily mortality rates for newly emerged adults, by fixing the temperature at 25 °C. This allows us to assess the mortality in newly emerged adults that will be sufficient to drive tsetse populations to extinction, when all other factors are kept at optimal levels. When daily mortality for newly emerged adults is 0.1% per-day, extinction probability, for a population starting with a single larva is 0.7, whereas, when the population starts with a single newly emerged adult, or a larvipositing female, the extinction probability is 0.35 for the same level of daily mortality rates among newly emerged adults (Fig 6.5 A and B). Any population starting with a single individual in any of the counting stages, will go extinct when daily mortality rates in newly emerged adults are as high as 15% per-day. As the sizes of the initial population increase to 100 each, extinction

probability stays at zero for daily mortality rates, for newly emerged adults, below 12% per-day. Substantially high levels of mortality are thus required to achieve extinction if mortality is increased only in newly emerged adults.

Control techniques that are presently being used for killing tsetse (such as tiny targets (Hargrove *et al.*, 2000; Esterhuizen *et al.*, 2006; Shaw *et al.*, 2015; Mbewe *et al.*, 2018*b*)) kill more larvipositing adults than immature adults, because the immature adult phase only lasts for about a week. Moreover, newly emerged adults have poorly developed thoracic musculature and low fat reserves, these two factors may limit their ability to fly the distances for them to be killed at stationary baits. Mobile baits such as insecticide treated cattle on the other hand, tend to be more effective in catching newly emerged adults than stationary targets (Hargrove, 1991). Hargrove *et al.* (1995) carried out a large-scale experiment that used odour baited traps to sample *G. m. morsitans* Westwood and *G.pallidipes* Austen in Zimbabwe. For both species, very small numbers of newly emerged flies compared to larvipositing adults were caught. Therefore, in theory, a sustained daily kill rate of about 3.5%, due to insecticide-impregnated targets, should be sufficient to eliminate closed populations of tsetse (Fig 6.5 A and B).

We calculated extinction probabilities as a function of daily mortality rates for larvipositing female adults experiencing a constant temperature of 25 °C. When the pioneer populations consist of single individuals of the three stages separately, and the daily mortality rate for larvipositing females is increased from 0.1% per-day to 3% per-day, extinction probabilities go to one at different rates, for different counting points.

6.7 Conclusion

The general model works for all counting points, for different decomposition of the recruitment rates between the life stages. We showed that extinction probability for different counting stages depends on the probability of recruitment between these stages. We showed that previous models used to estimate extinction probability for tsetse populations are special cases of the general model.

We can predict insect population persistence only if we count and calculate carefully, taking account of different stages. We caution that the basic reproduction number is not sufficient to accurately determine insect population persistence. Our results offer insights into population dynamics and provide tools that will help with more detailed

models of insect populations. Finally, we advise that demographic studies of insects should be clear about life stages and counting points.

Chapter 7

Estimating the intrinsic rate of natural increase for populations of tsetse (*Glossina* spp.) in a world of changing climate

7.1 Abstract

Climate change may already have altered the distribution in Africa of tsetse, *Glossina* spp. - vectors of trypanosomiases. We need to investigate the possibility of tsetse population extinction in areas that are now getting too hot for them, as well as the chances of them surviving in regions that were previously too cold but are now getting warmer. The intrinsic rate of natural increase, r_0, is a useful metric for determining the suitability of a set of environmental condition for population growth. The relatively simple life history of the tsetse allows us to solve the Euler-Lotka equation to obtain a closed form expression for r_0. We use *Glossina morsitans morsitans* Westwood population growth rate, estimated from a mark-recapture experiment, to compare the intrinsic growth rate estimates from our model, and we show that the two results compare well. We use daily average temperatures recorded at Rekomitjie Research Station, Zambezi Valley, Zimbabwe between 1960 and 2018 to calculate long-term average values of r_0. Our results show that the growth rate is positive and relatively stable during the cooler seasons, for most of the years of the study period. However, since 2010, tsetse population has been experiencing negative growths more frequently during the hot dry season (October-December). We created three climate change scenarios for the next 50 years, using daily average temperature data for 2018 as a baseline. We suggest that if daily average temperatures continue to increase at the

rate of 0.08°C per day in the Zambezi Valley, tsetse population could go extinct within the next 50 years.

7.2 Introduction

Tsetse (*Glossina* spp.) are vectors of human and animal trypanosomiases, neglected tropical diseases endemic in many sub-Saharan African countries. Sustained control efforts have reduced disease burden in the last 10 years (World Health Organization (WHO), 2018), but a recent study showed that climate warming may alter tsetse distribution in Africa (Lord *et al.*, 2018). Increasing temperatures could lead to local extinction of tsetse population in some regions, but could also lead to emergence of tsetse and trypanosomiasis in regions that were formerly too cold for the flies (Lord *et al.*, 2018). There is a need for an improved understanding of tsetse population growth as a function of field temperatures that fluctuate with season.

The intrinsic rate of natural increase, r_0, is an important metric in insect population dynamics as it can be used to determine whether or not a set of environmental condition is suitable for an insect population (Birch, 1948). Several attempts have been made to estimate the natural rate of increase for tsetse population from age distributions of samples of field caught flies, but these efforts largely dissipated following Van Sickle (1988) demonstration that they were invalid - and that valid estimations using age data were highly sensitive to sampling error. More recently, Williams *et al.* (1990) have used the Euler-Lotka equation to relate age-specific mortality and fecundity to overall growth rates of tsetse populations. Hargrove (2004) used this model to calculate tsetse growth rates as a function of (constant) environmental temperature. However, whereas it is a relatively simple matter to estimate the growth of tsetse populations at constant temperatures, nobody has estimated the intrinsic rate of increase for tsetse population as a function of fluctuating field temperatures.

At every instant in time, in environments that are unlimited by space or resources, the intrinsic rate of increase gives a good picture of the rate of increase per-head attainable in a population – given the combination of the mortality and fecundity rates as functions of various environmental factors, such as temperature, moisture etc. Note, however, that the actual growth rate of such populations may often lie below the intrinsic rate of natural increase, as factors such as density-dependent effects may hinder the population growth rate from attaining its full potential (Birch, 1948). A positive r_0 value implies that the combination of survival, reproduction and mortality rates in the population, is favourable for positive population growth. A negative r_0

value on the other hand indicates that the environment is unsuitable for the population to grow. In the latter case the population will go extinct if the negative r_0 value is sustained long enough.

A standard means of estimating the natural rate of increase for populations is the Euler-Lotka equation (Birch, 1948; Zidon *et al.*, 2015), given in discrete form as:

$$\sum \lambda^{-x} l_x m_x = 1. \tag{7.1}$$

where l_x is the probability at birth, that a female individual is alive at age x and m_x the expected number of female offspring produced in a unit time by a female aged x. The basic reproduction number R_o is:

$$R_o = \sum l_x m_x. \tag{7.2}$$

Tsetse have a relatively simple life history; they produce a single larva at regular intervals, which vary with temperature (Hargrove, 2003*b*). The mortality rate is higher in newly emerged adult flies than in mature adults, and mortality rates increase in females $>$ 60 days old (Hargrove, 2020). In most populations in the field, however, more than 80% of the female populations would have died before the first 60 days of adult life. Hence, flies older than 60 days do not play a major role in the population dynamics. We assumed that once flies enter the reproductive cycle, they produce new offspring with constant probability throughout their lives. The very basic life history of tsetse allows us to obtain a closed form solution of the Euler-Lotka equation to derive an expression for the intrinsic rate of natural increase for tsetse population living at constant temperature. We estimated the rate of increase per-head as a function of daily average temperature recorded at Rekomitjie Research Station, Zambezi Valley, Zimbabwe from 1960 to 2018, and we calculated long-term averages of the rate of increase. We then estimated the average annual growth rate over the next 50 years for each of three climate-warming scenarios (0.04°C, 0.06°C and 0.08°C annual increase), using measured daily temperatures for 2018 as a baseline.

7.3 Materials and Methods

We model the growth of populations of female tsetse: we ignore the male population, except to assume that there are always sufficient numbers of males present to ensure that all females are inseminated within about the first 7-10 days of their adult lives. We sub-divide the life cycle of female tsetse into three distinct stages – larval/pupal, pre-ovulation adult and larvipositing adult stages. Tsetse biology has been intensively

studied for more than a century and rates of birth, development, and mortality rates have been measured both in the laboratory and in the field (Rogers and Randolph, 1984*b*; Hargrove, 2004; Jarry *et al.*, 1999; Hargrove *et al.*, 2011; Hargrove and Vale, 2019). Using this knowledge, and taking advantage of the relatively simple life cycle, we develop a framework that allows us to solve the Euler-Lotka equation analytically for the intrinsic rate of increase of tsetse populations. We proceed by making the following simplifying assumptions.

7.4 Model assumptions

- Once the fly attains the age of first ovulation, she retains constant fecundity rate throughout her life.
- The life cycle of the fly is divided into three stages: larva, pre-ovulation adults and larvipositing adults.
- p_o is the probability of reaching the larviposition loop from birth
- p_c is the probability of reaching the point where offspring are counted, from the point of larviposition.
- c is the time interval (assumed constant) between successive births.
- p_l is the probability of surviving a larviposition loop.
- p_d is the probability of depositing a live larva.

Here birth refers to the time at which a larva is deposited.

7.5 Model

Suppose l_x is the probability of a female surviving from birth to age x, and that m_x is the mean number of female offspring produced in a unit time by a female aged x. Here age refers to the number of times a female completes a larviposition loop, incremented by the time interval between successive successive births.

7.5.1 Basic reproduction number

The basic reproduction number (R_o) can be calculated directly from equation (7.2):

$$R_0 = \sum l_x m_x,$$

$$x = c, 2c, 3c, ...$$

where

$$l_i = p_o p_l^i \tag{7.3}$$

and

$$m_i = p_d p_c \tag{7.4}$$

Therefore, from equations (7.2), (7.3), and (7.4),

$$R_0 = \sum_{x=1}^{\infty} l_x m_x = p_o p_l p_c p_d + p_d p_o p_l^2 p_c + p_d p_o p_l^3 p_c + ...$$

$$= \frac{p_o p_c p_l p_d}{(1 - p_l)}, \tag{7.5}$$

where $0 < p_l < 1$. Notice that R_o does not depend on c, moreover, if p_o or $p_c \to 0$, then $R_o \to 0$. This implies that whenever any of the parameters approach 0, the population goes extinct.

Equation (7.5) corresponds to the net reproduction number for tsetse population, in the general model presented (Are and Hargrove, 2020*a*).

7.5.2 The intrinsic rate of natural increase

We can calculate the intrinsic rate of natural increase r_0 from the Euler-Lotka equation. Suppose all parameter descriptions remain as above, we can rewrite equation (7.1) by letting $\lambda = e^{cr_0}$. Equation (7.1) then becomes:

$$\sum (e^{r_0 c})^{-T} l_T m_T = 1. \tag{7.6}$$

where T is the integer number of time steps.

Using equations (7.3) and (7.4), we can calculate r_0 directly from equation (7.6).

$$\sum_{T=1}^{\infty} (e^{r_0 c})^{-T} (p_c p_d)_T (p_o p_l)_T = 1,$$

solving for r_0 yields,

$$r_0 = (\frac{\ln[p_l(p_c p_o p_d + 1)]}{c}). \tag{7.7}$$

If p_o or $p_c p_d \to 0$, then $r_0 \to \frac{\ln[p_l]}{c}$. Since $0 < p_l < 1$, whenever any of the parameters approaches 0, r_0 becomes negative, which implies population extinction. Moreover, $r_0 = 0, \implies R_o = 1$.

7.5.3 Intrinsic growth rate as a function of temperature

We assume that key parameters are temperature dependent. The relationship between these parameters and temperature are given in detail in Are and Hargrove (2020*a*). We estimated the rate of increase on each day as a function of daily mean temperature, and we obtained the long-time (annual) average ($\hat{r_0}$) of r_0 by simple averaging across days.

7.5.4 Model validation

We compare growth rate estimates from the current model with the growth rate obtained from fitting an exponential function to a time series of estimates of tsetse numbers derived in the field. We use mark-recapture estimates of the numbers of female *Glossina morsitans morsitans* Westwood on Antelope Island, Lake Kariba, Zimbabwe (Hargrove and Williams, 1998) to calculate weekly growth rates for the population between January and December 1981. During this period the population was not subjected to any trapping pressures and was allowed to grow naturally, subject only to temperature and other meteorological effects.

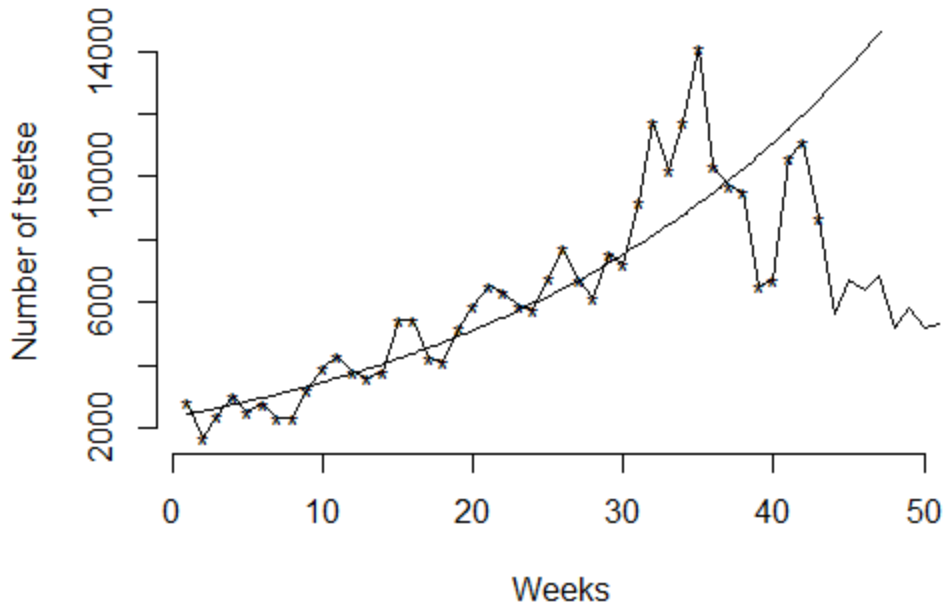

Figure 7.1: A fit of an exponential function to tsetse population data The vertical axis is the estimated *G. m. morsitans* female population on Antelope Island, Lake Kariba, Zimbabwe, from January 14th to December 30th, 1981. The time is measured in weeks, the smooth line shows the model fit, and the dots are the population estimates used in the fitting procedure.

We fitted an exponential function to the population estimates using the function *fit_easylinear()* from the R package "growthrate" (Figure 7.1). The weekly growth rate from the model fit is 0.0388 per week (95% CI [0.0336, 0.0439]). We then used the r_0 estimate to calculate the weekly growth rate as a function of the weekly average temperatures from January 14th to December 30th, 1981, and then calculated $\hat{r_0}$, the long-time average value of r_0 for the year. The $\hat{r_0}$ estimate from the model during this period is 0.0385 (95% CI [0.0345, 0.0425]). The two estimates, arrived at by two entirely independent methods, using quite different approaches, thus gave very similar estimates – indicating that the Euler-Lotka method provides a reasonable way of estimating mean growth rates over extended periods.

7.5.5 Sensitivity Analysis

In a recent study (Are and Hargrove, 2020*b*), an extensive sensitivity and uncertainty analysis was done on the extinction probabilities for populations of tsetse. The study derived an expression for the extinction probabilities for the flies' population and assessed the impact of each input parameter on the extinction probability. Here, in a

similar fashion to Are and Hargrove (2020*b*), we aim to determine the parameters that have the strongest impact on the magnitude of the intrinsic rate of natural increase r_0. Hence, we define probabilities p_l, p_c and p_o respectively as:
$p_l = e^{-\Psi\tau}$, $p_o = \epsilon e^{-\Omega\nu}$, $p_d = 1$ and $p_c = \beta e^{-\chi g}$, where:

- β : Probability a deposited larva is female
- χ : Pupal daily mortality
- ϵ: Probability of fertile insemination
- g: Pupal duration
- ν: Time from emergence to first ovulation
- Ω: Daily mortality in immature adults
- Ψ : Daily mortality in larvipositing adults
- τ: Inter-larval period

For the sensitivity analysis, we assume that the number of male tsetse in the population is always sufficient, such that all virgin females in the population are inseminated around the eighth day of their emergence as adults ($\epsilon = 1$).

We use the Latin Hypercube Sampling (LHS) method and obtain the Partial Rank Correlation Coefficient (PRCC) for the intrinsic growth rate with respect to all input parameters (See Are and Hargrove (2020*b*) for details on the methodology). Sensitivity analysis shows that the intrinsic rate, r_0, is most sensitive to daily mortality, Ψ, in larvipositing adults, followed by daily mortality, χ, in female pupae, and daily mortality, Ω, in immature adults. As expected, these three parameters, together with the inter-larval period, τ, and pupal duration, g, all have negative impact on r_0 (Fig 7.2). This again reinforces the conclusion reached in Are and Hargrove (2020*b*) that increasing daily adult mortality for female tsetse is the most effective way of controlling/eradicating populations of tsetse.

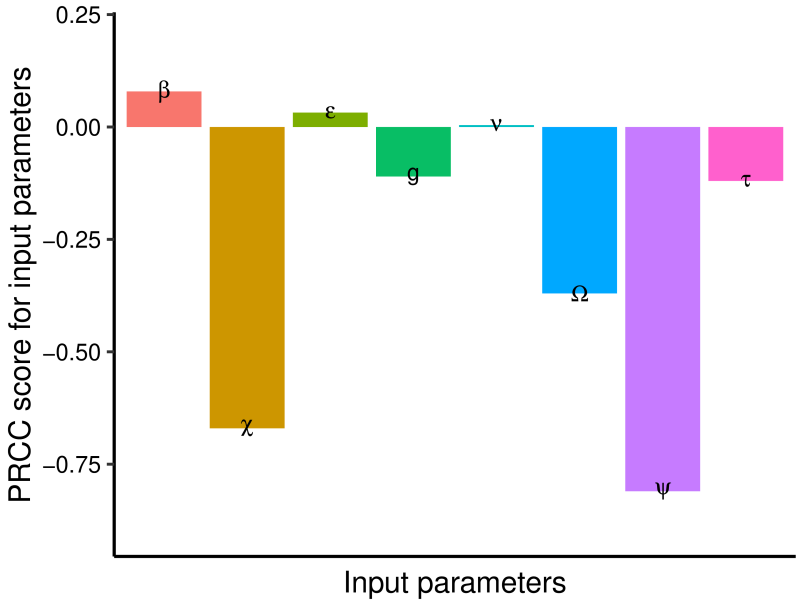

Figure 7.2: PRCC score for all eight model input parameters. β: probability a deposited larva is female, χ: pupal daily mortality, ϵ: probability of fertile insemination, g: pupal duration, ν: time from emergence to first ovulation, Ω: daily mortality in immature adults, Ψ: daily mortality in larvipositing adults, and τ: inter-larval period. Prior parameter distributions are taken from Table 3 of Are and Hargrove (2020*b*)

7.5.6 Temperature Data

Between November 1959 and December 2018, daily maximum and minimum temperatures have been recorded at Rekomitjie using a mercury thermometer placed in a Stevenson screen. Mean temperatures over 24-hour, and longer, periods were approximated using the average of the daily maximum and minimum temperatures. We present the annual mean temperature at Rekomitjie, from 1960-2018 (Fig 7.3). Annual mean temperatures fluctuate quite widely between years at Rekomitjie, but have remained consistently above 25°C since 1987. It is clear that Rekomitjie is getting hotter, and the rate at which the annual average temperatures depart from the optimal temperature for tsetse population growth (25°C) (Are and Hargrove, 2020*a*) has continued to increase.

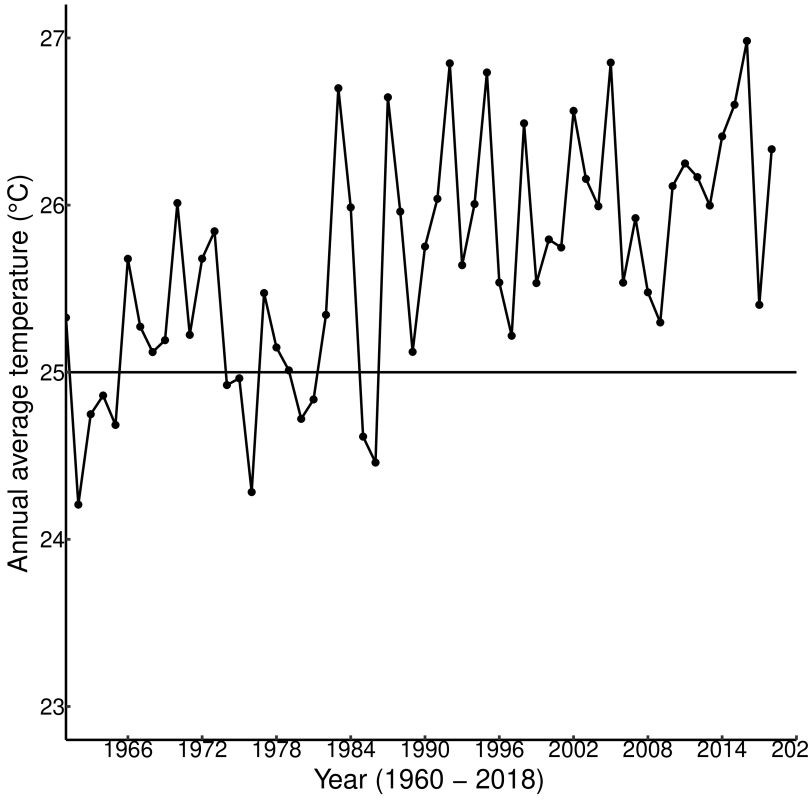

Figure 7.3: Annual mean temperature for Rekomitjie Research Station (1960-2018). The line through 25°C indicates the optimal temperature for tsetse population survival and reproduction.

We assess the differential changes in temperature between seasons for the study period. During the hot-wet season (January-April), the variation in monthly mean temperature has been minimal when compared to the fluctuation in the monthly mean temperature during the hot-dry season (September-December) where extreme temperature events have increased, both in intensity and in frequency (Fig 7.4 C). Further details about the temperature data are provided elsewhere (Lord *et al.*, 2018).

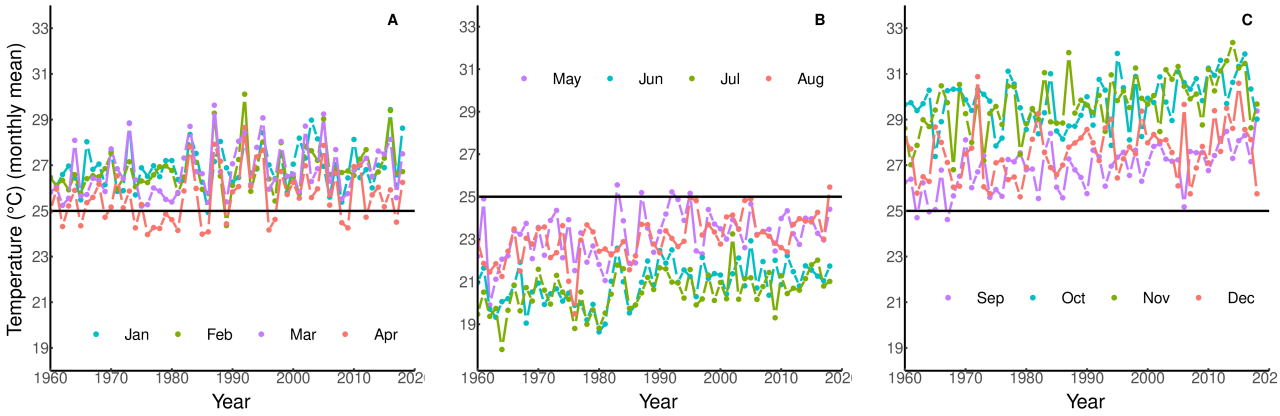

Figure 7.4: Monthly mean temperature at Rekomitjie for different seasons (1960 - 2018). Monthly average temperatures for months in A. the hot-wet season (January - April) B. cool-dry (May-August) and C. hot-dry (September-December). The line through 25°C indicates the optimal temperature for tsetse population survival and reproduction

7.5.7 Changes in age distributions with month of the year at Rekomitjie

High temperatures at Rekomitjie have serious implications for tsetse population dynamics. Studies have suggested that tsetse population age structure will be altered during the hot-dry seasons at Rekomitjie due to heat-induced mortality in pupae and newly emerged adults Hargrove (2013); Hargrove and Ackley (2015); Ackley and Hargrove (2017). An earlier study Van Sickle and Phelps (1988) suggested that the Rekomitjie population will seldom, if ever, achieve a stable age distribution because once disproportionate mortalities affect pupae and young adults during the hot-dry season, the age distribution will not stabilise before the next hot-dry season sets in. In this study, we investigate this matter further by analysing the data collected on the ovarian age distribution for *G. pallidipes* caught in traps at Rekomitjie from September 1988 – December 1999. We calculate the mean age of the population for consecutive months throughout the study period. Our results show that the mean age of the population is similar for months starting from February to August. However, from September to January, the mean age increases rapidly, indicating a large shift in the age distribution during the hot-dry season (Fig 7.5).

We compare the difference between the mean age of the population for the two consecutive months with one of the smallest (May - June), and largest (December - January) change in the mean age of the population, respectively. Essentially the age distributions in June and July have the same shape, whereas in December, the shape of the age distribution differs clearly from that of January.

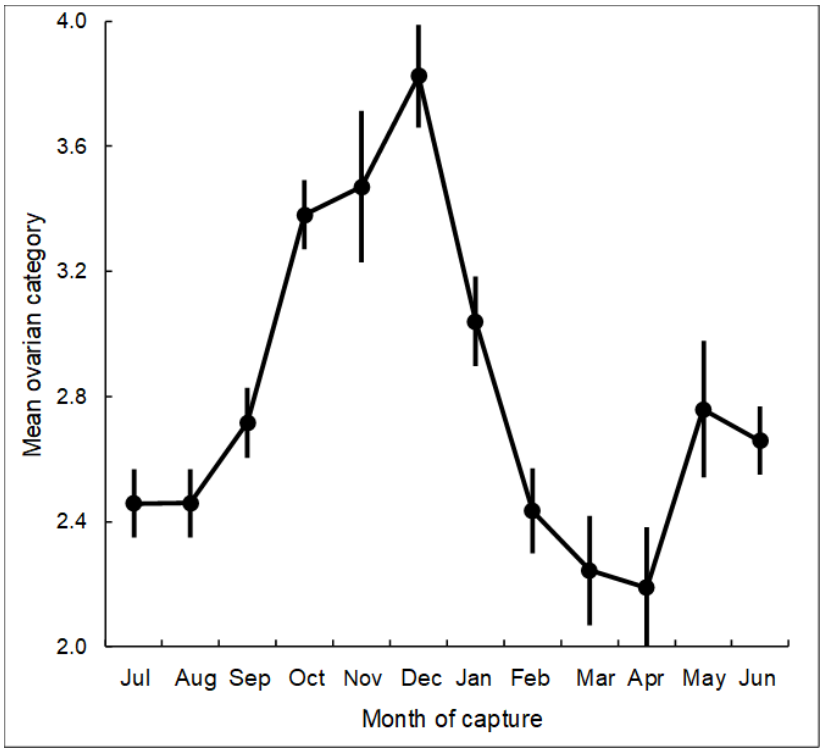

Figure 7.5: Changes in the mean ovarian category of adult female *G. pallidipes* captured using an electric net mounted on the back of an open pick-up. Error bars indicate the 95% confidence intervals for the mean. Flies captured at Rekomitjie Research Station, Zambezi Valley, Zimbabwe 1989-1993

7.5.8 Climate change scenarios

Over the past 27 years at Rekomitjie, average daily temperatures have increased by 2°C in the month of November, and by 0.9°C for the rest of the year (Lord *et al.*, 2018). Here we investigate the impact on the annual growth rates of tsetse population assuming that average temperatures continue to increase over the next 50 years at rates of either 0.04, 0.06 or 0.08 °C per-year. We are particularly interested to know what level of temperature increase would cause tsetse population growth rates to become consistently negative.

7.6 Results

We used the daily average temperature data and equation (7.7) to predict the intrinsic rate of natural increase of tsetse population in the neighbourhood of Rekomitjie, for each day between January 1960 and December 2018. We then calculated the annual averages for r_0. Notice that all references below to growth rates are values predicted from temperature profiles.

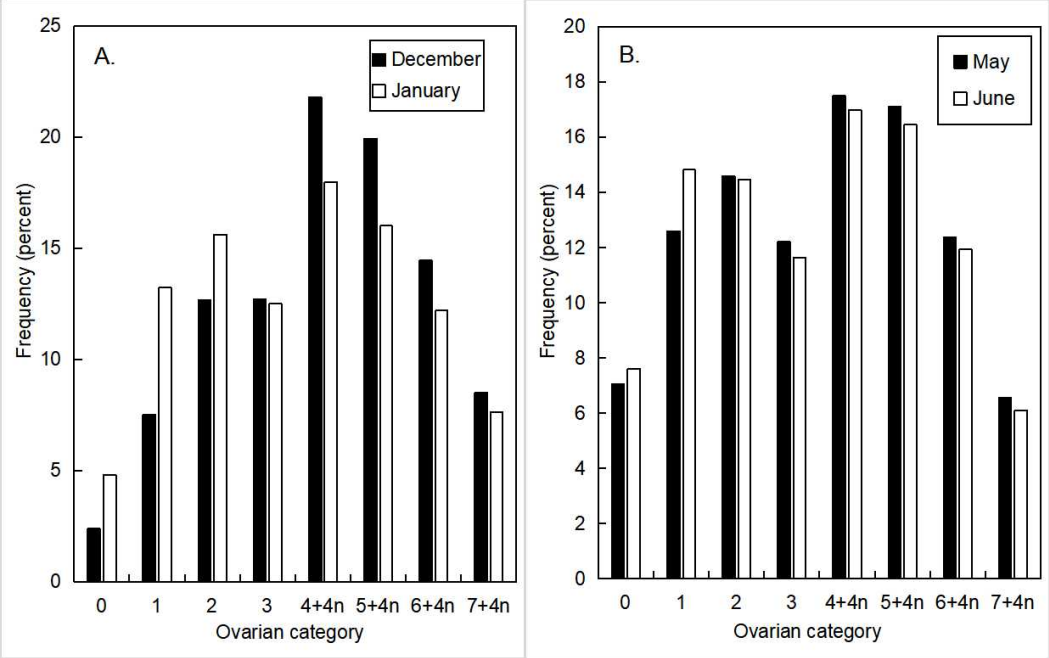

Figure 7.6: Ovarian age distributions for *G. pallidipes* caught in traps at Rekomitjie Research Station, September 1988 – December 1999. Graphs show results for months where there was the biggest (A) or smallest (B) change in mean age distribution between months. Samples sizes: December 8711; January 8887; May 9634; June 5574. Where n is a natural number

From 1960 to 1986, the annual average growth rate was relatively stable, varying between 0.0031 and 0.0039 per day. Between 1987 and 1995, however, the growth rate dropped below the previous minimum of 0.0031 per day in four of the nine years, with a low of 0.0029 per day in 1992, during which year catches of tsetse at Rekomitjie also fell to their lowest recorded levels up to that time (Hargrove and Ackley, 2015). There followed a slow recovery with increased growth rates until 2009. Thereafter, rates fell consistently, hitting an all-time low of 0.0023 per day in 2016 (Fig 7.7), at which time catches were also at an all-time low (Lord *et al.*, 2018).

Temperatures vary seasonally, and the highest temperatures at Rekomitjie are usually recorded at the end of the dry season in September–December. We classified the year into three seasons: hot-wet (January-April), cool-dry (May-August) and hot-dry (September-December). For each of these seasons we obtained the average growth for each month, separately, throughout the study period. This allowed us to assess the differential values of the average growth rate during the hot-dry months and the cooler seasons of the year. The average growth rate for January-April changed little over the years around an average value of 0.004, save for 1996 and 2016 when the average growth rate dropped markedly in January and February (Fig 7.8A).

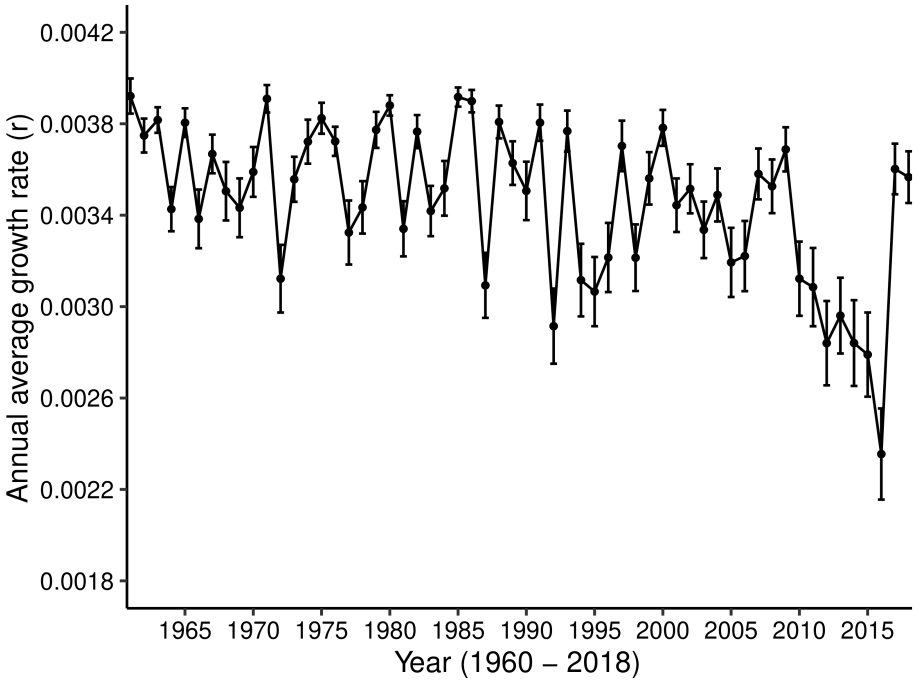

Figure 7.7: Averaged annual growth rates for tsetse population at Rekomitjie Research Station, Zambezi Valley, Zimbabwe: from 1960 to 2018.

For March-April, the average growth rate varied even less. The growth rate attains its highest value during this period, about 0.0045. The average growth rate was consistently lower during June and July, the coolest months of the year, than in May and August (Fig 7.8B).

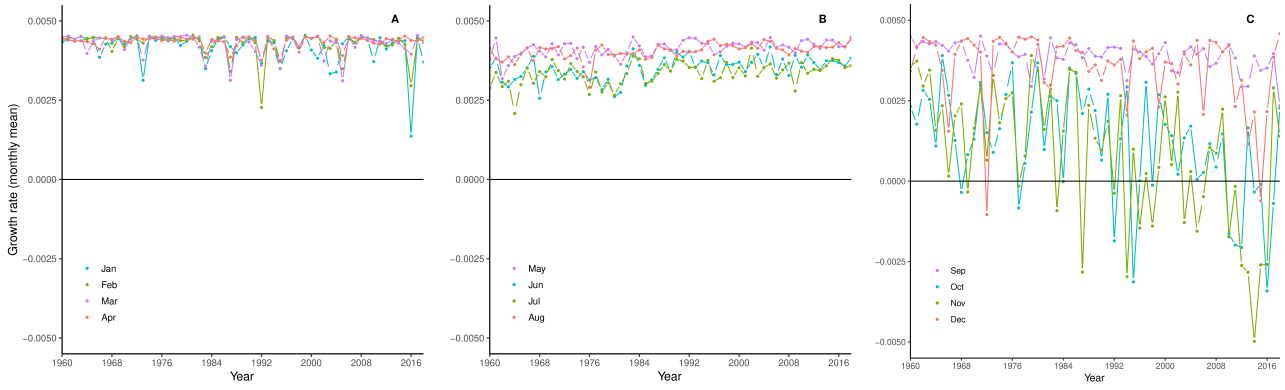

Figure 7.8: The average growth rate for different seasons from 1960 to 2018 (A). Average growth rate for January, February, March and April (B). Average growth rate for May, June, July and August (C). Average growth rate for September, October, November and December. The horizontal lines show the limit of positive growth; below those lines the population size decreases

By far the greatest variation in the average growth rate, both within and between years, occurs during the last four months of the year, particularly in October and November. Between 1987 and 2018, the average growth rate has been negative for 22 out of 32 years, during these two months. In 2014, the growth rate dipped below -0.005 per day - the lowest monthly average ever (Fig 7.8C). Variation in average growth rates for September were much less pronounced than for the other three months of the hot-dry season. From 2010 to 2018, there has been increased variation in the growth rate during the last three months of the year.

7.6.1 Projected growth rates at Rekomitjie assuming different rates of temperature increase

We created three climate change scenarios to predict changes over the next 50 years, using 2018's daily average temperature as the baseline. We used these temperature projections to calculate the annual average value of the growth rate from 2019-2068. When the warming rate is slow (at 0.04 °C per-year) the average growth rate continues

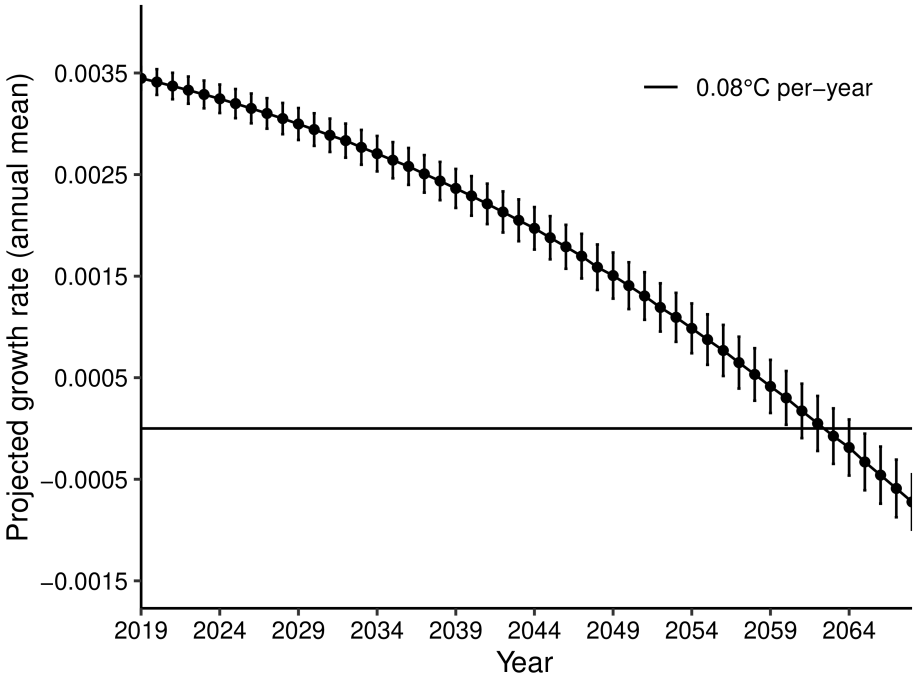

Figure 7.9: The annual average growth rate for the projected climate change scenario (0.08 °C per-year), from 2019 to 2068. The horizontal line, through the vertical axis, shows the point where the average growth rate attains negative values: indicating population extinction, if sustained. Error bars indicate the 95% confidence intervals for the mean. Extinction did not occur within the next 50 years for 0.04 and 0.06 warming rates, and we did not include these in out plot

to decline as temperature increases, but does not reach a negative value within the next 50 years. For the scenario where the warming rate is 0.06 °C per-year, the $\hat{r_0}$ drops below 0.001 but did not reach a negative value. It is only when the warming rate is increased to 0.08 °C per-year that $\hat{r_0}$ declines steadily until it reaches a negative value in 2063. If negative $\hat{r_0}$ values are sustained the population will eventually become extinct.

7.7 Discussion

It has been suggested that temperature increases at Rekomitjie led to a collapse in tsetse population in that region after 2010 (Lord *et al.*, 2018). The study suggested that, if temperatures continue to increase, there could be local extinctions of tsetse population in the Zambezi Valley. The current study used temperature data from Rekomitjie to estimate how tsetse growth rates have changed in the neighbourhood of the Station over the past 60 years. It also predicted the changes that will occur in future growth rates, given different climate change scenarios. We solved the Euler-Lotka equation analytically, and we obtained a closed form expression for the intrinsic growth rate, r_0, for tsetse populations. To validate our model results we used weekly average temperature readings for Antelope Island, Lake Kariba, Zimbabwe, in 1981, to estimate the average growth rate for 1981 for a population of *G. m. morsitans* on the island. We compared our results to the growth rate obtained by fitting an exponential function to weekly estimates of female tsetse population, over the same period (1981). Our model results compare well with the estimates from the exponential model fitted to the mark-recapture population estimates. This is expected because the tsetse population on the island in 1981 was growing from a low base and numbers were much lower than the carrying capacity. We expect, therefore, that density-dependent effects would not have been important. In this case, the actual population growth rate should be very close to the intrinsic rate of increase.

We used daily average temperatures recorded at Rekomitjie, from January 1960 to December 2018, to calculate the long-time average values of r_0. Using the temperature readings for 2018 as a baseline, we projected three climate change scenarios, by projecting daily average temperatures for Rekomitjie over the next 50 years, following three climate warming rates. We used the projected temperatures to calculate the long-time averages of the growth rate.

Our results show that annual population intrinsic growth rates for tsetse at Rekomitjie have fluctuated quite widely between years over the past 60 years, but there was no

strong trend in the rates between 1960 and about 2009. Thereafter, however, average temperatures have increased markedly, and annual average growth rate have declined, most sharply since 2010. Our results agree with several studies (Pagabeleguem *et al.*, 2016; Ackley and Hargrove, 2017), both empirical and theoretical, that have shown that high temperatures are devastating for tsetse populations, and that increasingly high temperatures can drive tsetse populations to extinction (Lord *et al.*, 2018; Are and Hargrove, 2020*a*). Our results offer insight into how very high temperatures during the hot-dry season are responsible for the decline in tsetse population at Rekomitjie. During the hot-dry seasons, high mortality rates in both pupal and newly emerged adult stages, due to high temperatures (Ackley and Hargrove, 2017), can explain the negative growth rates during these months. As global warming continues to increase the average temperatures at Rekomitjie all year round, tsetse populations will not be able to recover fully from the disastrous impact of the hot-dry season before the next hot-dry season sets in. This may possibly explain the decline in tsetse population, at Rekomitjie, over the past 10 - 20 years.

Our intrinsic growth rate estimates for Rekomitjie, on the other hand, may be seen as the upper bound for the actual population growth because of the following reasons: (1) Our modelling framework did not consider density-dependent effects. In practice, effects such as density-dependent mortality will limit population growth when the population approaches its carrying capacity. At these times the actual growth rate for tsetse populations will not attain its intrinsic capacity. (2) For tsetse populations in the field, where temperatures vary seasonally, the very high temperatures during the hot-dry season destabilise the population age distribution through the particularly high losses experienced by pupae and newly emerge adults under these conditions (Van Sickle and Phelps, 1988; Hargrove, 2013), thereby preventing the actual growth rate from reaching its full potential. We can then expect the actual population growth rate to fall below our r_0 estimates. The foregoing two reasons may explain why, despite the observed decrease in tsetse populations at Rekomitjie, the annual average intrinsic growth rate, although reducing, is still positive as at 2018. The fact that the r_0 is reducing shows that Rekomitjie is becoming less suitable for tsetse populations to thrive. Moreover, our model projections suggests that a warming rate of 0.08°C will be sufficient to ensure that the intrinsic growth rate will become negative and it will be impossible for any tsetse population to survive at Rekomitjie beyond about 2063.

We have shown that tsetse populations have very low growth rates. For instance, from the 1960s to 1980s where the environmental temperatures were relatively favourable throughout the year, the annual average growth rate was always below 0.004 per-year.

This is consistent with the low birth rates found in tsetse (Hargrove, 2004, 1988). Other studies have also estimated very low population growth rates for tsetse populations (Van Sickle and Phelps, 1988; Hargrove, 2004). We have assumed that no additional mortality is imposed on the study population either by control efforts or human activities e.g., bush clearing. If any of these assumptions are not true, tsetse growth rates will be lower than the values we predict here. Our result may therefore be a best-case scenario for tsetse populations which are experiencing the temperatures recorded at Rekomitjie during these periods. Our result can be seen as a maximum for the instantaneous growth rate attainable for tsetse populations at Rekomitjie.

We acknowledge that the Euler-Lotka equation was premised on the assumption that the population attains a stable age distribution, and where the environment is not limited by resources or space. Our results agree in part with findings from previous studies on tsetse age distribution (Van Sickle and Phelps, 1988; Hargrove, 2013; Hargrove and Ackley, 2015; Ackley and Hargrove, 2017), and also provide a clearer insight on what happens to tsetse age distribution within a year. We show that, although it is true that tsetse age distribution cannot be stable throughout each of the months in a year, as soon as the hot-dry season passes, tsetse age distribution essentially stabilises from February of the following year up until August before the high temperatures again perturb the age structure significantly between the next September and January. Amarasekare and Coutinho (2013) provided strong evidence that populations can still attain stationary age distributions as long as the fluctuation in environmental temperature is within a threshold that will allow reproduction and development processes to continue. We have shown that, for most months of the year at Rekomitjie, apart from the hot dry seasons, temperature variations have been modest. The instability in the age distribution is often introduced during the hot-dry seasons (Hargrove, 2013) of the very hot years. Therefore, barring any density-dependent effects, we would expect the actual growth rates to be close to the intrinsic rate of increase during seasons when population growth is optimal. Our estimates provide a very insightful first step towards more accurate estimates of tsetse population growth rate under varying temperatures.

The current study did not consider density-dependent effects, which are very important for tsetse populations (Rogers, 1975). However, the Euler-Lotka equation has been shown to yield comparable estimates of r_0 to other methods that do incorporate density-dependent effects (Cortés, 2016). Moreover, as tsetse populations continue to decline at Rekomitjie, due to high temperatures, density-dependent effects may fall off, since the population may lie far below its carrying capacity.

Amarasekare and Coutinho (2013) compared the average growth rate calculated from the Euler-Lotka equation to the one obtained from a stage-structured compartmental model. They reported that the growth rates obtained from the two methods were similar, deviating only when the juvenile developmental period is long (several months) and/or when projections involve long time-scales (> 50 years). When the two estimates differ, r_0 derived from the Euler-Lotka equation overestimates the true growth rates and, by implication, it overestimates population persistence. They suggested that the accuracy of r_0, from the Euler-Lotka method, declines if it is used to predict insect population extinction beyond a 50-year period. The current study took these cautions into account. Moreover, tsetse developmental period can vary between 20 - 60 days depending on temperature, and it therefore can be categorized as having a relatively short developmental period. In any case, the shortcoming of our method will be that we may have slightly overestimated the intrinsic rate of increase, and therefore tsetse populations may more likely go extinct earlier than in 2063 as predicted by our results.

7.8 Conclusions

The framework presented here is simple and relatively straightforward. We recognize that some of the shortcomings of our formulation may limit the accuracy of our estimates. However, among other things, since we got a closed form expression for r_0, it will serve as a metric for easy comparison with future findings. Moreover, it is clear that this crude estimate provides strong evidence that climate change could drive tsetse populations to extinction within the next 50 years (with a medium warming rate of 0.08°C per-year), especially in regions with temperature profiles similar to those at Rekomitjie. If our results are true for other insects with similar reproduction/development processes to tsetse, then several insects, of agricultural and/or economic importance, may be at risk of extinction in the Zambezi Valley in particular, and Zimbabwe (or other part of Africa with similar temperature regimes as the Zimbabwe), in general.

We are currently constructing an individual based model which will allow us to factor in several environmental variables at the same time, to estimate growth rate of tsetse populations in the wild.

Chapter 8

Conclusions

8.1 Summary

In this thesis, we set out to: (i) Improve estimates of extinction probabilities for populations of tsetse. (ii) Carry out a holistic sensitivity analysis on the parameters involved in the extinction probabilities, thereby informing tsetse control measures that can achieve tsetse eradication more effectively. (iii) Generalize the derivations of extinction probabilities for tsetse populations and provide key insights on insect demography. (iv) Estimate extinction probabilities as a function of fixed temperatures flies are experiencing, as well as in situations where temperatures vary during the life cycle of the flies. In what follows, we summarize the key findings of each of the study objectives as presented in the five journal articles (three are already published, and two are almost ready for submission), which make up the basis of this work.

In Chapter 3, we identified a shortcoming of earlier estimates of extinction probabilities for tsetse populations, which involved a restrictive assumption that female tsetse produce male and female offspring with equal probabilities. We presented a framework that allowed us to estimate extinction probabilities in more realistic situations where the probability of producing a female larva can be anywhere in the interval (0,1). We estimated extinction probabilities as a function of the probability a deposited larva is female, and showed that extinction probability is minimum when there are slightly more females in the population than males. Furthermore, we showed that a daily mortality rate of 3.5% among adult females is sufficient to eradicate any closed populations of tsetse. This level of mortality can be achieved, in some tsetse species, simply by deploying control techniques such as insecticide treated targets or cattle. These affordable methods can be used to achieve tsetse and trypanosomiasis eradication. (This work is published as Kajunguri *et al.* (2019)).

In Chapter 4, we carried out global uncertainty and sensitivity analysis on extinction probabilities after deriving extinction probability in a more compact form with fewer mathematical steps. Sensitivity analysis showed that extinction probability is more sensitive to daily mortality rates for adult female than for any other factor affecting tsetse mortality or natality. This was true in all of the scenarios we considered in the global sensitivity analysis. We went further to analyse the impact of combining control measures on tsetse extinction probabilities and times to extinction. We provided evidence suggesting that local sensitivity increases with increase in the size of the initial population. We also showed that a newly proposed method termed Boosted SIT (BSIT), which combines SIT with a juvenile hormone analogue, such as pyriproxyfen, may not offer any significant benefit over the cheap traditional methods targeting the survival of adult female flies. We called for further work to evaluate the cost effectiveness benefit of BSIT over traditional methods, such as insecticide treated targets. Our model suggests, conversely, that increasing adult and pupal mortality simultaneously could offer some benefit. However, no study has yet proposed a suitable method to achieve this. Finally, we concluded that control efforts that achieve high mortality rates in adult female offer the single most effective approach to eradicating tsetse populations. (This work is published as Are and Hargrove (2020*b*))

In Capter 5, we derived extinction probabilities as a function of different levels of fixed temperatures. Our modelling framework captured the disparity between daily mortality rates in newly emerged adults and mature adult flies. This made our model more realistic as the mortality rate is considerably higher in newly emerged adults compared to mature flies (Ackley and Hargrove, 2017). Our results suggest 25°C as the optimal temperature for tsetse population growth. We showed that no tsetse population can survive when subjected to sustained temperatures below 16 °C or above 32 °C. We suggest that, as average temperatures continue to increase in Africa, tsetse populations could go extinct in places that are already getting too hot for the flies. A recent forewarning of such a situation has been seen at Rekomitjie Research Station, in the Zambezi Valley of Zimbabwe (Lord *et al.*, 2018). In the other hand places that have been too cool for the flies in the past, may become warm enough in the near future for tsetse to survive and transmit trypanosomiasis. We concluded that future tsetse control plans should account for possible impacts of climate change on tsetse population dynamics. This work is published as (Are and Hargrove, 2020*a*).

In Chapter 6, we developed a general model that can be used to estimate extinction probabilities for tsetse populations regardless of our assumptions around the life stages of the individuals in the initial population. We showed that previous models used to

estimate tsetse population persistence are special cases of the generalized framework that we have developed here. Our results suggest that the basic reproduction number is independent of the counting points chosen. By contrast, estimated extinction probabilities change with the probability of recruitment from one life stage to the other. We showed, however, that when tsetse populations are large, any of the life stages can be used, as a proxy in the modelling framework, to estimate tsetse population persistence. This is because the extinction probabilities converge to the same points when initial population sizes increase. However, as populations decline the counting point becomes very important and this should be accounted for when estimating extinction probabilities in such situations. This work is in preparation for publication as Are *et al.* (2020).

Finally in Chapter 7, the simple life history of tsetse allowed us to make simplifying assumptions that enabled us to derive an analytical expression for the intrinsic rate of increase for tsetse populations as a function of temperature. To validate our model, we compared the intrinsic rate of increase for tsetse populations on Antelope Island, Lake Kariba, Zimbabwe, estimated using daily average temperatures, and the growth rate estimates obtained from fitting an exponential curve to population estimates obtained using mark-recapture. We showed that the two results are comparable. We went further to investigate tsetse age distributions as temperatures vary seasonally. We showed that tsetse populations will attain a new stable age distribution within few months after the population is perturbed, during the hot-dry seasons, by a disproportionate mortality in pupae and newly emerged adults. Finally, we created various climate change scenarios by assuming different annual warming rates using 2018 average daily temperature for Rekomitjie as a baseline. We found that an annual warming rate of 0.08 °C will make the neighbourhood of Rekomitjie unsuitable for tsetse populations within the next 50 years, and that tsetse populations could go extinct there.

8.2 Future work

As global temperature and other meteorological variables continue to change, there is increasing interest in the effects of climate on the distribution and abundance of insect species – particularly vectors of disease. Accordingly, increased efforts are now being focused on estimating the effects of climate change on tsetse population dynamics and the allied effects on the epidemiology of trypanosomiasis. Much work has been carried out to improve understanding of tsetse populations dynamics in field situations. These studies often assume that tsetse populations are closed – free from invasion from surrounding patches. Moreover, existing works often consider temperature as the only

environmental driver of tsetse population dynamics in their modelling framework. In reality, tsetse populations are not closed in most field situations, and other meteorological factors, such as humidity and rainfall, are also important in tsetse population dynamics. To address these shortcomings, we envisage future work where we will develop a meta-population individual-based model that will allow movements between tsetse patches. The model will also account for other environmental factors, such as humidity and rainfall. We will use climate data from Rekomitjie Research Station, Zambezi Valley, Zimbabwe to develop this model. This new modelling framework will offer more realistic estimates of tsetse population persistence in changing environments. It will also provide clearer insights on several key factors in tsetse population dynamics, such as tsetse age structure and tsetse mortality rates in field situations where climatic factors vary both over a 24-hour cycle and also seasonally.

Bibliography

Abd-Alla, A.M., Bergoin, M., Parker, A.G., Maniania, N.K., Vlak, J.M., Bourtzis, K., Boucias, D.G. and Aksoy, S. (2013). Improving Sterile Insect Technique (SIT) for tsetse flies through research on their symbionts and pathogens. *Journal of Invertebrate Pathology*, vol. 112, pp. S2–S10.

Ackley, S.F. and Hargrove, J.W. (2017). A dynamic model for estimating adult female mortality from ovarian dissection data for the tsetse fly Glossina pallidipes Austen sampled in Zimbabwe. *PLoS Neglected Tropical Diseases*, vol. 11, no. 8.

Adams, B.M., Banks, H.T., Banks, J.E. and Stark, J.D. (2005). Population dynamics models in plant-insect herbivore-pesticide interactions. *Mathematical Biosciences*, vol. 196, no. 1, pp. 39–64.

Alderton, S., Macleod, E.T., Anderson, N.E., Palmer, G., Machila, N., Simuunza, M., Welburn, S.C. and Atkinson, P.M. (2018). An agent-based model of tsetse fly response to seasonal climatic drivers: Assessing the impact on sleeping sickness transmission rates. *PLoS Neglected Tropical Diseases*, vol. 12, no. 2.

Amarasekare, P. and Coutinho, R.M. (2013). The intrinsic growth rate as a predictor of population viability under climate warming. *Journal of Animal Ecology*, vol. 82, no. 6, pp. 1240–1253.

Are, E.B., Dushoff, J. and Hargrove, J.W. (2020). Insect demography: does it matter if we count babies or mummies? *In preparation.*

Are, E.B. and Hargrove, J.W. (2020*a*). Extinction probabilities as a function of temperature for populations of tsetse (Glossina spp.). *PLoS Neglected Tropical Diseases*, vol. 14, no. 5, p. e0007769.

Are, E.B. and Hargrove, J.W. (2020*b*). Uncertainty and sensitivity analyses of extinction probabilities suggest that adult female mortality is the weakest link for populations of tsetse (Glossina spp). *PLoS Neglected Tropical Diseases*, vol. 14, no. 5, p. e0007854.

Artzrouni, M. and Gouteux, J.P. (2003). Estimating tsetse population parameters: application of a mathematical model with density-dependence. *Medical and Veterinary Entomology*, vol. 17, no. 3, pp. 272–279.

Axelrod, D. and Kimmel, M. (2015). *Branching processes in biology*. Springer-Verlag.

Barclay, H.J., Hargrove, J.W. and van den Driessche, P. (2020*a*). Estimating tsetse fertility: daily averaging versus periodic larviposition. *Medical and Veterinary Entomology*, vol. 34, no. 1, pp. 27–33.

Barclay, H.J., Hargrove, J.W. and van den Driessche, P. (2020*b*). Modelling optimal timing and frequency of insecticide sprays for eradication or knockdown of closed populations of tsetse flies Glossina spp.(Diptera: Glossinidae). *Medical and Veterinary Entomology*, vol. 34, no. 2, pp. 151–163.

Barclay, H.J. and Vreysen, M.J.B. (2011). A dynamic population model for tsetse (Diptera: Glossinidae) area-wide integrated pest management. *Population Ecology*, vol. 53, no. 1, pp. 89–110.

Bartlett, M.S. (1949). Some evolutionary stochastic processes. *Journal of the Royal Statistical Society. Series B (Methodological)*, vol. 11, no. 2, pp. 211–229.

Beier, J.C. (1998). Malaria Parasite development in Mosquitoes. *Annual Review of Entomology*, vol. 43, pp. 519–43.

Birch, L.C. (1948). The Intrinsic Rate of Natural Increase of an Insect Population. *Journal of Animal Ecology*, vol. 17, no. 1, pp. 15–26.

Blower, S.M. and Dowlatabadi, H. (1994). Sensitivity and uncertainty analysis of complex models of disease transmission: an hiv model, as an example. *International Statistical Review/Revue Internationale de Statistique*, pp. 229–243.

Bourn, D., Reid, R., Rogers, D., Snow, B., Wint, W. *et al.* (2001). Environmental change and the autonomous control of tsetse and trypanosomosis in sub-Saharan Africa. *Environmental Research Group Oxford Limited, Oxford, UK*.

Bursell, E., Gough, A.J.E., Beevor, P.S., Cork, A., Hall, D.R. and Vale, G.A. (1988). Identification of components of cattle urine attractive to tsetse flies, Glossina spp.(Diptera: Glossinidae). *Bulletin of Entomological Research*, vol. 78, no. 2, pp. 281–291.

Burt, A. (2014). Heritable strategies for controlling insect vectors of disease. *Philosophical Transactions of the Royal Society B: Biological Sciences*, vol. 369, no. 1645, pp. 1–8.

Büscher, P., Cecchi, G., Jamonneau, V. and Priotto, G. (2017). Human African trypanosomiasis. *The Lancet*, vol. 390, no. 10110, pp. 2397–2409.

Cecilia, H., Arnoux, S., Picault, S., Dicko, A., Seck, M.T., Sall, B., Bassène, M., Vreysen, M., Pagabeleguem, S., Bancé, A. *et al.* (2019). Environmental heterogeneity drives tsetse fly population dynamics and control. *BioRxiv*, p. 493650.

Challier, A. (1982). The ecology of tsetse (Glossina spp.)(Diptera, Glossinidae): a review (1970–1981). *International Journal of Tropical Insect Science*, vol. 3, no. 2-3, pp. 97–145.

Chigusa, Y., Ohshita, M., Taya, J., Kirinoki, M., Yokoi, H., Kawai, S. and Matsuda, H. (1997). Relationship between longevity and body weight in Glossina morsitans morsitans. *Medical Entomology and Zoology*, vol. 48, no. 2, pp. 91–96.

Childs, S.J. (2013). A set of discrete formulae for the performance of a tsetse population during aerial spraying. *Acta Tropica*, vol. 125, no. 2, pp. 202–213.

Chitnis, N., Hyman, J.M. and Cushing, J.M. (2008). Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model. *Bulletin of Mathematical Biology*, vol. 70, no. 5, pp. 1272–1296.

Chowell, G., Castillo-Chavez, C., Fenimore, P.W., Kribs-Zaleta, C., Arriola, L. and Hyman, J.M. (2004). Implications of an uncertainty and sensitivity analysis for SARS's basic reproductive number for general public health measures. *Emerging Infectious Diseases, to appear*.

Clemons, A., Mori, A., Haugen, M., Severson, D.W. and Duman-Scheel, M. (2010). Culturing and egg collection of Aedes aegypti. *Cold Spring Harbor Protocols*, vol. 5, no. 10, pp. 1–5.

Collins, J.M. (2011). Temperature variability over africa. *Journal of Climate*, vol. 24, no. 14, pp. 3649–3666.

Conrad, K.F., Woiwod, I.P. and Perry, J.N. (2002). Long-term decline in abundance and distribution of the garden tiger moth (Arctia caja) in Great Britain. *Biological Conservation*, vol. 106, pp. 329–337.

Cortés, E. (2016). Perspectives on the intrinsic rate of population growth. *Methods in Ecology and Evolution*, vol. 7, no. 10, pp. 1136–1145.

Cuissance, D. (1989). Glossines et trypanosomes. *Master international Erasmus/Comett/Alfa sur les Maladies parasitaires tropicales. Valençia (Spain)*, p. 115 and appendices.

Dransfield, R., Brightwell, R., Kiilu, J., Chaudhury, M. and Ad Abie, D.A. (1989). Size and mortality rates of Glossina pallidipes in the semi-arid zone of southwestern kenya. *Medical and Veterinary Entomology*, vol. 3, no. 1, pp. 83–95.

Edney, R.B. and Barrass, E.B. (1962). The body temperature of the Tsetse fly, Glossina Morsitans Westwood (Diptera, Muscidae). *Journal of Insect Physiology*, vol. 8, pp. 469–481.

Esterhuizen, J., Kappmeier Green, K., Nevill, E.M. and Van Den Bossche, P. (2006). Selective use of odour-baited, insecticide-treated targets to control tsetse flies Glossina austeni and

G. brevipalpis in South Africa. *Medical and Veterinary Entomology*, vol. 20, no. 4, pp. 464–469.

Esterhuizen, J., Rayaisse, J.B., Tirados, I., Mpiana, S., Solano, P., Vale, G.A., Lehane, M.J. and Torr, S.J. (2011). Improving the cost-effectiveness of visual devices for the control of riverine tsetse flies, the major vectors of human african trypanosomiasis. *PLoS Neglected Tropical Diseases*, vol. 5, no. 8.

Fall, A.A., Bouyer, J. and Lancelot, R. (2011). Development of a mathematical model for tsetse population dynamic to optimize the control in the niayes (senegal). CIRAD.

Feller, W. (1968). *An introduction to probability theory and its applications*. John Wiley & Sons.

Franco, J.R., Simarro, P.P., Diarra, A. and Jannin, J.G. (2014). Epidemiology of human African trypanosomiasis. *Clinical Epidemiology*, vol. 6, no. 1, pp. 257–275.

Gaston, K.A. and Randolph, S.E. (1993). Reproductive under-performance of tsetse flies in the laboratory, related to feeding frequency. *Physiological entomology*, vol. 18, no. 2, pp. 130–136.

Glasgow, J.P. (1963). The distribution and abundance of tsetse. *Pergamon Press, Oxford*.

Gouteux, J.P., Artzrouni, M. and Jarry, M. (2001). A density-dependent model with reinvasion for estimating tsetse fly populations (diptera: Glossinidae) through trapping. *Bulletin of Entomological Research*, vol. 91, no. 3, pp. 177–183.

Habel, J.C., Segerer, A., Ulrich, W., Torchyk, O., Weisser, W.W. and Schmitt, T. (2015). Butterfly community shifts over two centuries. *Conservation Biology*, vol. 30, no. 4, pp. 754–762.

Hallmann, C.A., Sorg, M., Jongejans, E., Siepel, H., Hofland, N., Sumser, H., Ho, T., Schwan, H., Stenmans, W., Mu, A., Goulson, D. and Kroon, H.D. (2017). More than 75 percent decline over 27 years in total flying insect biomass in protected areas. *PLoS One*, vol. 12, no. 10.

Hargrove, J.W. (1981). Discrepancies between estimates of tsetse fly populations using mark-recapture and removal trapping techniques. *Journal of Applied Ecology*, pp. 737–748.

Hargrove, J.W. (1988). Tsetse: the limits to population growth. *Medical and Veterinary Entomology*, vol. 2, no. 3, pp. 203–217.

Hargrove, J.W. (1990). Age-dependent changes in the probabilities of survival and capture of the tsetse, Glossina morsitans morsitans Westwood. *International Journal of Tropical Insect Science*, vol. 11, no. 3, pp. 323–330.

Hargrove, J.W. (1991). Ovarian ages of tsetse flies (Diptera: Glossinidae) caught from mobile and stationary baits in the presence and absence of humans. *Bulletin of Entomological Research*, vol. 81, no. 1, pp. 43–50.

Hargrove, J.W. (1993). Target barriers for tsetse flies (Glossina spp.)(diptera: Glossinidae): quick estimates of optimal target densities and barrier widths. *Bulletin of Entomological Research*, vol. 83, no. 2, pp. 197–200.

Hargrove, J.W. (1994). Reproductive rates of tsetse flies in the field in Zimbabwe. *Physiological Entomology*, vol. 19, no. 4, pp. 307–318.

Hargrove, J.W. (1995). Towards a general rule for estimating the stage of pregnancy in field-caught tsetse flies. *Physiological Entomology*, vol. 20, no. 3, pp. 213–223.

Hargrove, J.W. (1999). Reproductive abnormalities in tsetse flies in Zimbabwe. *Entomologia Experimentalis et Applicata*, vol. 92, no. 1, pp. 89–99.

Hargrove, J.W. (2000). A theoretical study of the invasion of cleared areas by tsetse flies (diptera: Glossinidae). *Bulletin of Entomological Research*, vol. 90, no. 3, pp. 201–209.

Hargrove, J.W. (2001*a*). Factors affecting density-independent survival of an island population of tsetse flies in Zimbabwe. *Entomologia Experimentalis et Applicata*, vol. 100, no. 2, pp. 151–164.

Hargrove, J.W. (2001*b*). Mark–recapture and moran curve estimates of the survival probabilities of an island population of tsetse flies Glossina morsitans morsitans (diptera: Glossinidae). *Bulletin of Entomological Research*, vol. 91, no. 1, pp. 25–35.

Hargrove, J.W. (2001*c*). The effect of temperature and saturation deficit on mortality in populations of male Glossina m. morsitans (Diptera: Glossinidae) in Zimbabwe and Tanzania. *Bulletin of Entomological Research*, vol. 91, no. 2, pp. 79–86.

Hargrove, J.W. (2003*a*). Optimized simulation of the control of tsetse flies Glossina pallidipes and G. m. morsitans (Diptera: Glossinidae) using odour-baited targets in Zimbabwe. *Bulletin of Entomological Research*, vol. 93, no. 1, pp. 19–29.

Hargrove, J.W. (2003*b*). *Tsetse eradication: sufficiency, necessity and desirability.* DFID Animal Health Programme, Centre for Tropical Veterinary Medicine.

Hargrove, J.W. (2004). Tsetse population dynamics. In: *The Trypanosomiases, CABI Publishing*, pp. 113–135.

Hargrove, J.W. (2005). Extinction probabilities and times to extinction for populations of tsetse flies Glossina spp. (Diptera: Glossinidae) subjected to various control measures. *Bulletin of Entomological Research*, vol. 95, no. 1, pp. 13–21.

Hargrove, J.W. (2012). Age-specific changes in sperm levels among female tsetse (Glossina spp.) with a model for the time course of insemination. *Physiological Entomology*, vol. 37, no. 3, pp. 278–290.

Hargrove, J.W. (2013). An example from the world of tsetse flies. *Mathematical Biosciences and Engineering*, vol. 10, no. 3, pp. 691–704.

Hargrove, J.W. (2020). A model for the relationship between wing fray and chronological and ovarian ages in tsetse (Glossina spp). *Medical and Veterinary Entomology*.

Hargrove, J.W. and Ackley, S.F. (2015). Mortality estimates from ovarian age distributions of the tsetse fly Glossina pallidipes Austen sampled in Zimbabwe suggest the need for new analytical approaches. *Bulletin of Entomological Research*, vol. 105, no. 3, pp. 294–304.

Hargrove, J.W., English, S., Torr, S.J., Lord, J., Haines, L.R., Van Schalkwyk, C., Patterson, J. and Vale, G. (2019). Wing length and host location in tsetse (Glossina spp.): Implications for control using stationary baits. *Parasites and Vectors*, vol. 12, no. 1, pp. 1–13.

Hargrove, J.W., Holloway, M.T.P., Vale, G.A., Gough, A.J.E. and Hall, D.R. (1995). Catches of tsetse (Glossina spp.)(Diptera: Glossinidae) from traps and targets baited with large doses of natural and synthetic host odour. *Bulletin of Entomological Research*, vol. 85, no. 2, pp. 215–227.

Hargrove, J.W. and Langley, P.A. (1990). Sterilizing tsetse (diptera: Glossinidae) in the field: a successful trial. *Bulletin of Entomological Research*, vol. 80, no. 4, pp. 397–403.

Hargrove, J.W. and Langley, P.A. (1993). A field trial of pyriproxyfen-treated targets as an alternative method for controlling tsetse (diptera: Glossinidae). *Bulletin of Entomological Research*, vol. 83, no. 3, pp. 361–368.

Hargrove, J.W., Omolo, S., Msalilwa, J.S. and Fox, B. (2000). Insecticide-treated cattle for tsetse control: The power and the problems. *Medical and Veterinary Entomology*, vol. 14, no. 2, pp. 123–130.

Hargrove, J.W., Ouifki, R. and Ameh, J.E. (2011). A general model for mortality in adult tsetse (Glossina spp.). *Medical and Veterinary Entomology*, vol. 25, no. 4, pp. 385–394.

Hargrove, J.W., Ouifki, R., Kajunguri, D., Vale, G.A. and Torr, S.J. (2012). Modeling the control of trypanosomiasis using trypanocides or insecticide-treated livestock. *PLoS Neglected Tropical Diseases*, vol. 6, no. 5.

Hargrove, J.W. and Vale, G.A. (2019). Models for the rates of pupal development, fat consumption and mortality in tsetse (Glossina spp). *Bulletin of Entomological Research*, pp. 1–15.

Hargrove, J.W. and Williams, B.G. (1998). Optimized simulation as an aid to modelling, with an application to the study of a population of tsetse flies, Glossina morsitans morsitans (Diptera: Glossinidae). *Bulletin of Entomological Research*, vol. 88, no. 4, pp. 425–435.

Harris, T.E. (1965). The Theory of Branching Processes. *A report prepared for United States Air force Project Rand*, vol. 7, no. R-381-PR, pp. 79–80.

Helton, J.C., Iman, R.L. and Brown, J.B. (1985). Sesnitivity analysis of the asymptotic behavior of a model for the environmental movement of radionuclides. *Ecological Modelling*, vol. 28, pp. 243–278.

Hoare, A., Regan, D.G. and Wilson, D.P. (2008). Sampling and sensitivity analyses tools (sasat) for computational modelling. *Theoretical Biology and Medical Modelling*, vol. 5, no. 1, p. 4.

Hocking, K.S., Lamerton, J.F. and Lewis, E.A. (1963). Tsetse-fly control and eradication. *Bulletin of the World Health Organization*, vol. 28, no. 5-6, p. 811.

Ilyinykh, A. (2011). Analysis of the causes of declines in Western Siberian outbreaks of the nun moth Lymantria monacha. *BioControl*, vol. 56, pp. 123–131.

Iman, R.L., Helton, J.C. and Campbell, J.E. (1981). An approach to sensitivity analysis of computer models: Part I—Introduction, input variable selection and preliminary variable assessment. *Journal of Quality Technology*, vol. 13, no. 3, pp. 174–183.

Intergovernmental Panel on Climate Change (IPCC) (2007). Working Group III Fourth Assessment Report. *Technical Report*.

Jacob, C. (2010). Branching processes: their role in epidemiology. *International Journal of Environmental Research and Public Health*, vol. 7, no. 3, pp. 1186–1204.

Jagers, P. (1995). Branching processes as population dynamics. *Bernoulli*, vol. 1, no. 1-2, pp. 191–200.

Jarry, M., Gouteux, J.-P. and Khaladi, M. (1999). Estimation of age-dependent survival rates of female tsetse flies (diptera: Glossinidae) from ovarian age distributions. *Bulletin of Entomological Research*, vol. 89, no. 6, pp. 515–521.

Jarry, M., Khaladi, M. and Gouteux, J.-P. (1996). A matrix model for studying tsetse fly populations. *Entomologia Experimentalis et Applicata*, vol. 78, no. 1, pp. 51–60.

Kajunguri, D., Are, E.B. and Hargrove, J.W. (2019). Improved estimates for extinction probabilities and times to extinction for populations of tsetse (Glossina spp). *PLoS Neglected Tropical Diseases*, vol. 13, no. 4, pp. 1–15.

Kent, E., Neumann, S., Kummer, U. and Mendes, P. (2013). What can we learn from global sensitivity analysis of biochemical systems? *PLoS One*, vol. 8, no. 11.

Kgori, P., Modo, S. and Torr, S.J. (2006). The use of aerial spraying to eliminate tsetse from the okavango delta of botswana. *Acta Tropica*, vol. 99, no. 2-3, pp. 184–199.

Kioy, D., Jannin, J. and Mattock, N. (2004). Human African trypanosomiasis. *Nature Reviews Microbiology*, vol. 2, no. 3, pp. 186–187.

Kleynhans, E. and Terblanche, J.S. (2011). Complex interactions between temperature and relative humidity on water balance of adult tsetse (Glossinidae, Diptera): implications for climate change. *Frontiers in Physiology*, vol. 2, p. 74.

Lange, K. (2010). *Applied probability*. Springer Science & Business Media.

Lange, K., Boehnke, M. and Carson, R. (1981). Moment computations for subcritical branching processes. *Journal of Applied Probability*, vol. 18, no. 1, pp. 52–64.

Langley, P.A., Felton, T., Stafford, K.E. and Oouchp, H. (1990). Formulation of pyriproxyfen, a juvenile hormone mimic, for tsetse control. *Medical and Veterinary Entomology*, vol. 4, no. 2, pp. 127–133.

Langley, P.A., Felton, T.E. and Oouchi, H. (1988). Juvenile hormone mimics as effective sterilants for the tsetse fly Glossina morsitans morsitans. *Medical and Veterinary Entomology*, vol. 2, no. 1, pp. 29–35.

Laroche, L. (2017). *Optimiser la technique de l'insecte stérile chez les Glossines: étude du transfert de pyriproxifène du mâle stérile à la femelle en conditions expérimentales*. Ph.D. thesis, MSc Thesis 1st year progress report.

Laroche, L., Ravel, S., Baldet, T., Lancelot, R., Chandre, F., Rossignol, M., Fafet, J.-F. and Bouyer, J. (2018). Assessment of the boosted sit approach using pyriproxyfen on tsetse in laboratory conditions.

Leak, S.G. (1999). *Tsetse biology and ecology: their role in the epidemiology and control of trypanosomosis*. ILRI (aka ILCA and ILRAD).

Lehane, M., Alfaroukh, I., Bucheton, B., Camara, M., Harris, A., Kaba, D., Lumbala, C., Peka, M., Rayaisse, J.B., Waiswa, C. *et al.* (2016). Tsetse control and the elimination of gambian sleeping sickness. *PLoS Neglected Tropical Diseases*, vol. 10, no. 4.

Lejon, V., Jacobs, J. and Simarro, P.P. (2013). Elimination of sleeping sickness hindered by difficult diagnosis. *Bulletin of World Health Organization*, vol. 91, p. 718.

Lin, S., DeVisser, M.H. and Messina, J.P. (2015). An agent-based model to simulate tsetse fly distribution and control techniques: a case study in nguruman, kenya. *Ecological Modelling*, vol. 314, pp. 80–89.

Linden, M.E.L. (1984). Effect of temperature on the reproduction of Glossina pallidipes, with reference to G. m. morsitans. *Entomologia Experimentalis et Applicata*, vol. 36, no. 1, pp. 77–83.

Lindh, J.M., Goswami, P., Blackburn, R.S., Arnold, S.E., Vale, G.A., Lehane, M.J. and Torr, S.J. (2012). Optimizing the colour and fabric of targets for the control of the tsetse fly Glossina fuscipes fuscipes. *PLoS Neglected Tropical Diseases*, vol. 6, no. 5.

Lindh, J.M., Torr, S.J., Vale, G.A. and Lehane, M.J. (2009). Improving the cost-effectiveness of artificial visual baits for controlling the tsetse fly Glossina fuscipes fuscipes. *PLoS Neglected Tropical Diseases*, vol. 3, no. 7.

Lister, B.C. and Garcia, A. (2018). Climate-driven declines in arthropod abundance restructure a rainforest food web. *PNAS*, vol. 2015.

Lord, J.S., Hargrove, J.W., Tor, S.J. and Vale, G.A. (2018). Climate change and African trypanosomiasis vector populations in Zimbabwe's Zambezi Valley : A mathematical modelling study. *PLoS Medicine*, pp. 1–18.

Lord, J.S., Mthombothi, Z., Lagat, V.K., Atuhaire, F. and Hargrove, J.W. (2017). Host-seeking efficiency can explain population dynamics of the tsetse fly Glossina morsitans morsitans in response to host density decline. *PLoS Neglected Tropical Diseases*, vol. 11, no. 7, p. e0005730.

Madsen, T., Wallace, D.I. and Zupan, N. (2013). Seasonal fluctuation in tsetse fly populations and human african trypanosomiasis: A mathematical model. In: *BIOMAT 2012*, pp. 56–69. World Scientific.

Madubunyi, L.C. (1975). A technique for detecting abortions in wild populations of Glossina species: Sterility principle for insect control. pp. 477–485. Proceedings of a Symposium on the Sterility Principle for Insect Control or Eradication Jointly Organized by the IAEA and FAO and Held in Innsbruck 22–26 July. *International Atomic Energy Agency*, Vienna.

Madubunyi, L.C. (1978). Relative frequency of reproductive abnormalities in a natural population of Glossina morsitans morsitans Westwood (Diptera: Glossinidae) in Zambia. *Bulletin of Entomological Research*, vol. 68, no. 3, pp. 437–442.

Marino, S., Hogue, I.B., Ray, C.J. and Kirschner, D.E. (2008). A methodology for performing global uncertainty and sensitivity analysis in systems biology. *Journal of Theoretical Biology*, vol. 254, no. 1, pp. 178–196.

Matsuyama, R., Akhmetzhanov, A.R., Endo, A., Lee, H., Yamaguchi, T., Tsuzuki, S. and Nishiura, H. (2018). Uncertainty and sensitivity analysis of the basic reproduction number of diphtheria: a case study of a Rohingya refugee camp in Bangladesh, November–December 2017. *PeerJ*, vol. 6, p. e4583.

Mbewe, N.J., Saini, R.K., Torto, B., Irungu, J., Yusuf, A.A. and Pirk, C. (2018*a*). Effects of vector control on the population structure of tsetse (Glossina fuscipes fuscipes) in western Kenya. *Acta Tropica*, vol. 179, pp. 1–9.

Mbewe, N.J., Saini, R.K., Torto, B., Irungu, J., Yusuf, A.A. and Pirk, C.W. (2018*b*). Sticky small target: an effective sampling tool for tsetse fly Glossina fuscipes fuscipes Newstead, 1910. *Parasites & Vectors*, vol. 11, no. 1, p. 268.

McKay, M.D., Beckman, R.J. and Conover, W.J. (2000). A comparison of three methods for selecting values of input variables in the analysis of output from a computer code. *Technometrics*, vol. 42, no. 1, pp. 55–61.

Moore, S., Shrestha, S., Tomlinson, K.W. and Vuong, H. (2012). Predicting the effect of climate change on african trypanosomiasis: integrating epidemiology with parasite and vector biology. *Journal of the Royal Society Interface*, vol. 9, no. 70, pp. 817–830.

Muller, G., Grébaut, P. and Gouteux, J.P. (2004). An agent-based model of sleeping sickness: simulation trials of a forest focus in southern cameroon. *Comptes Rendus Biologies*, vol. 327, no. 1, pp. 1–11.

Mutika, G.N., Kabore, I., Parker, A.G. and Vreysen, M.J. (2014). Storage of male Glossina palpalis gambiensis pupae at low temperature: effect on emergence, mating and survival. *Parasites & Vectors*, vol. 7, no. 1, p. 465.

Muzari, M.O. and Hargrove, J.W. (2005). Artificial larviposition sites for field collections of the puparia of tsetse flies Glossina pallidipes and G. m. morsitans (Diptera: Glossinidae). *Bulletin of Entomological Research*, vol. 95, no. 3, p. 221.

Nilsson, S.G., Franzén, M. and Jönsson, E. (2017). Long-term land-use changes and extinction of specialised butterflies. *Insect Conservation and Diversity (2008)*, vol. 1, no. September 2008, pp. 197–207.

Nnko, H.J., Ngonyoka, A., Salekwa, L., Estes, A.B., Hudson, P.J., Gwakisa, P.S. and Cattadori, I.M. (2017). Seasonal variation of tsetse fly species abundance and prevalence of trypanosomes in the maasai steppe, tanzania. *Journal of Vector Ecology*, vol. 42, no. 1, pp. 24–33.

Öckinger, E. and Smith, H.G. (2007). Semi-natural grasslands as population sources for pollinating insects in agricultural landscapes. *Journal of Applied Ecology*, vol. 44, pp. 50–59.

Okiwelu, S.N. (1977*a*). Host preference and trypanosome infection rates of Glossina morsitans morsitans Westwood in the Republic of Zambia. *Annals of Tropical Medicine & Parasitology*, vol. 71, no. 1, pp. 101–107.

Okiwelu, S.N. (1977*b*). Insemination, pregnancy and suspected abortion rates in a natural population of Glossina morsitans morsitans (diptera: Glossinidae) in the republic of zambia. *Journal of Medical Entomology*, vol. 14, no. 1, pp. 19–23.

Ollerton, J., Winfree, R. and Tarrant, S. (2011). How many flowering plants are pollinated by animals? *Oikos*, vol. 120, no. 321, pp. 321–326.

Omondi, O.L., Wang, C. and Xue, X. (2015). Sensitivity and uncertainty analysis of a simplified Kirschner-Panetta model for immunotherapy of tumor-immune interaction. *Advances in Difference Equations*, vol. 2015, no. 1.

Pagabeleguem, S., Ravel, S., Dicko, A.H., Vreysen, M.J., Parker, A., Takac, P., Huber, K., Sidibé, I., Gimonneau, G. and Bouyer, J. (2016). Influence of temperature and relative humidity on survival and fecundity of three tsetse strains. *Parasites and Vectors*, vol. 9, no. 1, pp. 1–13.

Peck, S.L. (2012). Networks of habitat patches in tsetse fly control: Implications of metapopulation structure on assessing local extinction probabilities. *Ecological Modelling*, vol. 246, pp. 99–102.

Peck, S.L. and Bouyer, J. (2012). Mathematical Modeling, Spatial Complexity, and Critical Decisions in Tsetse Control. *Journal of Economic Entomology*, vol. 105, no. 5, pp. 1477–1486.

Pelton, E.M., Schultz, C.B., Jepsen, S.J., Black, S.H. and Crone, E.E. (2019). Western Monarch Population Plummets : Status, Probable Causes, and Recommended Conservation Actions. *Frontiers in Ecology and Evolution*, vol. 7.

Phelps, R.J. (1973). The effect of temperature on fat consumption during the puparial stages of Glossina morsitans morsitans Westwood (Dipt., Glossinidae) under laboratory conditions, and its implication in the field. *Bulletin of Entomological Research*, vol. 62, no. 3, pp. 423–438.

Phelps, R.J. and Burrows, P.M. (1969*a*). Prediction of the pupal duration of Glossina morsitans orientalis Vanderplank under field conditions. *Journal of Applied Ecology*, pp. 323–337.

Phelps, R.J. and Burrows, P.M. (1969*b*). Puparial duration in Glossina morsitans orientalis under conditions of constant temperature. *Entomologia Experimentalis et Applicata*, vol. 12, pp. 33–43.

Phelps, R.J. and Clarke, G.P.Y. (1974). Seasonal elimination of some size classes in males of Glossina morsitans morsitans Westwood (Diptera, Glossinidae). *Bulletin of Entomological Research*, vol. 64, no. 2, pp. 313–324.

Potts, S.G., Biesmeijer, J.C., Kremen, C., Neumann, P., Schweiger, O. and Kunin, W.E. (2010). Global pollinator declines : trends, impacts and drivers. *Trends in Ecology & Evolution*, vol. 25, no. 6, pp. 345–353.

Ramos-Elorduy, J., Manuel, J., Moreno, P., Prado, E.E., Perez, M.A., Otero, J.L. and Guevara, O.L.D. (1997). Nutritional Value of Edible Insects from the State of Oaxaca , Mexico. *Journal of Food Composition and Analysis*, vol. 157, no. 10, pp. 142–157.

Rayaisse, J.B., Esterhuizen, J., Tirados, I., Kaba, D., Salou, E., Diarrassouba, A., Vale, G.A., Lehane, M.J., Torr, S.J. and Solano, P. (2011). Towards an optimal design of target for tsetse control: comparisons of novel targets for the control of palpalis group tsetse in west africa. *PLoS Neglected Tropical Diseases*, vol. 5, no. 9.

Reid, R.S., Kruska, R.L., Deichmann, U., Thornton, P.K. and Leak, S.G.A. (2000). Human population growth and the extinction of the tsetse fly. *Agriculture, Ecosystems and Environment*, vol. 77, pp. 227–236.

Rogers, D.J. (1975). Ecology of Glossina. Natural regulation and movement of tsetse fly populations. In: *Revue d'elevage et de medecine veterinaire des pays tropicaux. Supplement. Les moyens de lutte contre les trypanosomes et leurs vecteurs. Actes du Colloque, Paris*, pp. 35–38.

Rogers, D.J. (1990). A general model for tsetse populations. *International Journal of Tropical Insect Science*, vol. 11, no. 3, pp. 331–346.

Rogers, D.J. and Randolph, S.E. (1984*a*). From a case study to a theoretical basis for tsetse control. *International Journal of Tropical Insect Science*, vol. 5, no. 5, pp. 419–423.

Rogers, D.J. and Randolph, S.E. (1984*b*). From a case study to a theoretical basis for tsetse control. *International Journal of Tropical Insect Science*, vol. 5, no. 05, pp. 419–423.

Rogers, D.J. and Randolph, S.E. (1984*c*). Local variation in population dynamics of G palpalis I Natural population regulation. *Bulletin of Entomological Research*, , no. 74, pp. 403–423.

Rogers, D.J. and Randolph, S.E. (1984*d*). A review of density-dependent processes in tsetse populations. *International Journal of Tropical Insect Science*, vol. 5, no. 5, pp. 397–402.

Rogers, D.J. and Robinson, T.P. (2004). Tsetse distribution: in The Trypanosomiases (Eds. Maudlin I., Holmes P.H. and Miles P.H.). In: *The Trypanosomiases, CABI Publishing*, p. 139–179.

RStudioTeam (2016). RStudio: Integrated Development for R. *RStudio, Inc., Boston, MA*.

Saini, R.K. and Hassanali, A. (1992). Olfactory sensitivity of tsetse to phenolic kairomones. *International Journal of Tropical Insect Science*, vol. 13, no. 1, pp. 95–104.

Samsuzzoha, M.D., Singh, M. and Lucy, D. (2013). Uncertainty and sensitivity analysis of the basic reproduction number of a vaccinated epidemic model of influenza. *Applied Mathematical Modelling*, vol. 37, no. 3, pp. 903–915.

Sanchez, M.A. and Blower, S.M. (1997). Uncertainty and sensitivity analysis of the basic reproductive rate: tuberculosis as an example. *American Journal of Epidemiology*, vol. 145, no. 12, pp. 1127–1137.

Sedda, L., Mweempwa, C., Ducheyne, E., De Pus, C., Hendrickx, G. and Rogers, D.J. (2014). A bayesian geostatistical moran curve model for estimating net changes of tsetse populations in zambia. *PLoS One*, vol. 9, no. 4.

Shaw, A.P., Tirados, I., Mangwiro, C.T., Esterhuizen, J., Lehane, M.J., Torr, S.J. and Kovacic, V. (2015). Costs of using "tiny targets" to control Glossina fuscipes fuscipes, a vector of gambiense sleeping sickness in Arua District of Uganda. *PLoS Neglected Tropical Diseases*, vol. 9, no. 3.

Shaw, A.P., Torr, S.J., Waiswa, C., Cecchi, G., Wint, G.R., Mattioli, R.C. and Robinson, T.P. (2013). Estimating the costs of tsetse control options: An example for Uganda. *Preventive Veterinary Medicine*, vol. 110, no. 3-4, pp. 290–303.

Solano, P., Torr, S.J. and Lehane, M.J. (2013). Is vector control needed to eliminate gambiense human African trypanosomiasis? *Frontiers in Cellular and Infection Microbiology*, vol. 3, p. 33.

Steverding, D. (2008). The history of African trypanosomiasis. *Parasites & Vectors*, vol. 1, no. 1, pp. 1–8.

Takken, W. and Weiss, M. (1978). The sterile insect technique for control of tsetse flies in africa. *IAEA Bulletin*, vol. 20, no. 3, p. 21.

Terblanche, J.S., Clusella-Trullas, S., Deere, J.A. and Chown, S.L. (2008). Thermal tolerance in a south-east African population of the tsetse fly Glossina pallidipes (Diptera, Glossinidae): implications for forecasting climate change impacts. *Journal of Insect Physiology*, vol. 54, no. 1, pp. 114–127.

Terblanche, J.S., Deere, J.A., Clusella-Trullas, S., Janion, C. and Chown, S.L. (2007). Critical thermal limits depend on methodological context. *Proceedings of the Royal Society B: Biological Sciences*, vol. 274, no. 1628, pp. 2935–2943.

Tirados, I., Esterhuizen, J., Kovacic, V., Mangwiro, T.C., Vale, G.A., Hastings, I., Solano, P., Lehane, M.J. and Torr, S.J. (2015). Tsetse control and gambian sleeping sickness; implications for control strategy. *PLoS Neglected Tropical Diseases*, vol. 9, no. 8.

Tobias, N.J. (2016). Insect Vectors of Disease : Untapped Reservoirs for New Antimicrobials? *Frontires in Microbiology*, vol. 7, no. December, pp. 1–5.

Torr, S.J. and Hargrove, J.W. (1999). Behaviour of tsetse (Diptera: Glossinidae) during the hot season in Zimbabwe: the interaction of micro-climate and reproductive status. *Bulletin of Entomological Research*, vol. 89, no. 4, pp. 365–379.

Turner, D.A. and Snow, W.F. (1984). Reproductive abnormality and loss in natural populations of Glossina pallidipes Austen (Diptera: Glossinidae) in Kenya. *Bulletin of Entomological Research*, vol. 74, no. 2, pp. 299–309.

Vale, G.A. (1971). Artificial refuges for tsetse flies (Glossina spp.). *Bulletin of Entomological Research*, vol. 61, no. 2, pp. 331–350.

Vale, G.A. (1993). Development of baits for tsetse flies (Diptera: Glossinidae) in Zimbabwe. *Journal of Medical Entomology*, vol. 30, no. 5, pp. 831–842.

Vale, G.A., Hall, D.R. and Gough, A.J.E. (1988*a*). The olfactory responses of tsetse flies, Glossina spp.(Diptera: Glossinidae), to phenols and urine in the field. *Bulletin of Entomological Research*, vol. 78, no. 2, pp. 293–300.

Vale, G.A. and Hargrove, J.W. (2015). Predicting the effect of climate change on the abundance and distribution of tsetse flies. *SACEMA Quarterly*.

Vale, G.A., Hargrove, J.W., Cockbill, G.F. and Phelps, R.J. (1986). Field trials of baits to control populations of Glossina morsitans morsitans westwood and G. pallidipes austen (diptera: Glossinidae). *Bulletin of Entomological Research*, vol. 76, no. 2, pp. 179–193.

Vale, G.A., Hargrove, J.W., Lehane, M.J., Solano, P. and Torr, S.J. (2015). Optimal strategies for controlling riverine tsetse flies using targets: a modelling study. *PLoS Neglected Tropical Diseases*, vol. 9, no. 3.

Vale, G.A., Lovemore, D.F., Flint, S. and Cockbill, G.F. (1988*b*). Odour-baited targets to control tsetse flies, Glossina spp.(Diptera: Glossinidae), in Zimbabwe. *Bulletin of Entomological Research*, vol. 78, no. 1, pp. 31–49.

Vale, G.A. and Torr, S.J. (2004). Development of bait technology to control tsetse. *In: The Trypanosomiases (Eds. Maudlin I., Holmes P.H., & Miles P.H.)*, pp. 509–523.

Vale, G.A. and Torr, S.J. (2005). User-friendly models of the costs and efficacy of tsetse control: application to sterilizing and insecticidal techniques. *Medical and Veterinary Entomology*, vol. 19, no. 3, pp. 293–305.

Van Sickle, J. (1988). Invalid estimates of rate of population increase from Glossina (Diptera: Glossinidea) age distributions. *Bulletin of Entomological Research*, vol. 78, pp. 155–161.

Van Sickle, J. and Phelps, R.J. (1988). Age distributions and reproductive status of declining and stationary populations of Glossina pallidipes Austen (Diptera: Glossinidae) in Zimbabwe. *Bulletin of Entomological Research*, vol. 78, no. 1, pp. 51–61.

van Swaay, C., van Strien, A., Harpke, A., Fontaine, B., Stefanescu, C., Roy, D., Kühn, E., Õnuao, E., Regan, E., Švitra, G. *et al.* (2013). The european grassland butterfly indicator: 1990–2011. *EEA Technical Reports*, vol. 11.

Vreysen, M.J., Saleh, K.M., Ali, M.Y., Abdulla, A.M., Zhu, Z.-R., Juma, K.G., Dyck, V.A., Msangi, A.R., Mkonyi, P.A. and Feldmann, H.U. (2000). Glossina austeni (diptera: Glossinidae) eradicated on the island of unguja, zanzibar, using the sterile insect technique. *Journal of Economic Entomology*, vol. 93, no. 1, pp. 123–135.

Vreysen, M.J., Seck, M.T., Sall, B. and Bouyer, J. (2013). Tsetse flies: their biology and control using area-wide integrated pest management approaches. *Journal of Invertebrate Pathology*, vol. 112, pp. S15–S25.

Wamwiri, F.N. and Changasi, R.E. (2016). Tsetse Flies (Glossina) as Vectors of Human African Trypanosomiasis : A Review. *BioMed Research International*, vol. 2016, pp. 1–8.

Welburn, S.C. and Coleman, P. (2015). Human and animal african trypanosomiasis. *One Health: The Theory and Practice of Integrated Health Approaches*, p. 201.

Williams, B.G., Dransfield, R.D. and Brightwell, R. (1990). Tsetse fly (Diptera: Glossinidae) population dynamics and the estimation of mortality rates from life-table data. *Bulletin of Entomological Research*, vol. 80, no. 4, pp. 479–485.

Williams, D. (1991). *Probability with martingales*. Cambridge university press.

World Health Organization (WHO) (2018). Trypanosomiasis, human African (sleeping sickness).
Available at: `https://www.who.int/news-room/fact-sheets/detail/trypanosomiasis-human-african-(sleeping-sickness)`

World Health Organization (WHO) (2020). Human African trypanosomiasis.
Available at: `https://www.who.int/news-room/fact-sheets/detail/trypanosomiasis-human-african-(sleeping-sickness)`

Ylioja, T., Roininen, H., Ayres, M.P., Rousi, M. and Price, P.W. (1999). Host-driven population dynamics in an herbivorous insect. *Proceedings of the National Academy of Sciences of the United States of America*, vol. 96, no. 19, pp. 10735–10740.

Zidon, R., Tsueda, H., Morin, E. and Morin, S. (2015). Projecting pest population dynamics under global warming: the combined effect of inter- and intra-annual variations. *Ecological Applications*, vol. 26, no. 4, pp. 1198–1210.