A modified model of the population dynamics of mosquitoes

by

Faith Ann Bjork

A Thesis Submitted to the
Graduate Faculty in Partial Fulfillment of the
Requirements for the Degree of
MASTER OF SCIENCE

Major: Biomedical Engineering

Iowa State University
Ames, Iowa

1981

TABLE OF CONTENTS

ABSTRACT

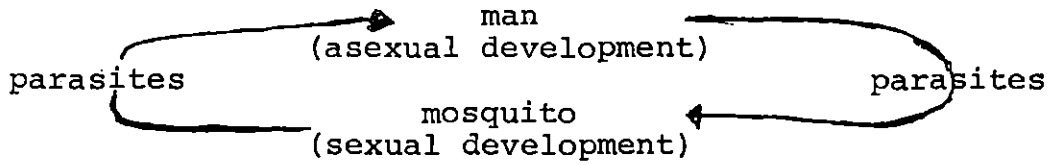
Macdonald's sporozoite rate model for a mosquito population was examined by investigating how each term influenced the value of s, the sporozoite rate. The sporozoite rate was found most responsive to p, the probability of survival for one day for a random mosquito. Gillies and Wilkes (1965) suggested that p is not a constant with respect to time as Macdonald assumed, but rather a time-dependent function. To further investigate this assumption, data for three mosquito populations collected by Gillies and Wilkes in 1965 were analyzed. A new time-dependent model was proposed for the survival curve. This model was incorporated into Macdonald's sporozoite rate equation to develop a more generalized form. The new sporozoite rate equation was tested with Gillies' and Wilkes' field values. The results indicated that the new survival curve model was an acceptable substitution to place in Macdonald's model. More field tests are necessary to further evaluate its reliability.

I. INTRODUCTION AND BACKGROUND

A. Malaria - Etiologic Agent

Malaria is a parasitic infection of vertebrates, caused by several species of protozoa (a phylum of acelluar animals) belonging to the genus Plasmodium (Garnham, 1966). The species of Plasmodium that naturally infect man are P. vivax, P. falciparium, P. malariae, and P. ovale (Garnham, 1966). All four species demonstrate parallel life cycles although each causes a clinically distinct disease.

The life cycle of Plasmodium (See Figure 1) is complex. It alternates between sexual and asexual generations. The different generations of the parasite require two different hosts, invertebrate and vertebrate. Sporogony, the mitotic generation of sporozoites occurs in the invertebrate host. This is termed the "extrinic" cycle. This work will deal with the genus of mosquito, Anopheles and its interaction with the vertebrate, man.



1. Intrinsic cycle (asexual generation)

When an infected mosquito feeds on a vertebrate host, it releases sporozoites into the blood of its host. The sporozoites congregate in the liver and enter the liver

cells. At this time, sporozoites are designated tissue schizonts and mitotically multiply extensively, for 5 to 15 days, depending on the species. After the schizont matures it ruptures its host cell and releases many new individuals, termed "merozoites" into the blood stream (Coatney et al., 1971). "The progeny of the final schizont of this exo-erythrocytic cycle (from a single sporozoite of Plasmodium) may be numbered in less than a hundred, in several thousands or in millions, according to the genus of the parasite" (Garnham, 1966).

Depending on the species of Plasmodium, the merozoites will act one of two ways. The merozoite may enter another liver cell and continue to multiply or the merozoite may enter a red blood cell (rbc); phagocytes destroy merozoites they capture. A merozoite inside a rbc continues with asexual multiplication. However, this time, the asexual growth will produce 36 or less new merozoites. (Number produced are species specific.) When a schizont reaches maturity the rbc membrane ruptures and releases a new brood of merozoites. These merozoites will follow one of two courses of development. The merozoite may penetrate another rbc and repeat the previous cycle or it may develop into a gametocyte. The rbc's containing gametocytes continue to circulate in the blood, waiting for a mosquito to ingest them in its next meal and repeat the cycle over again (Garnham, 1966).

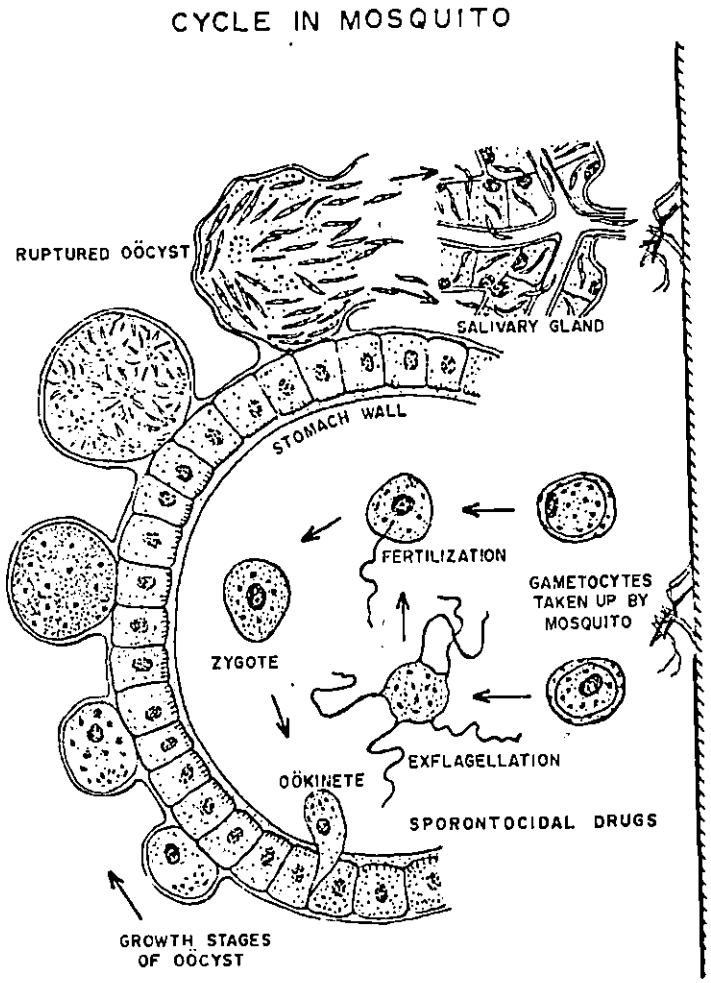


Figure 1. Life cycle of Plasmodium, the malaria parasite (Alvarado and Bruce-Chwatt, 1962)

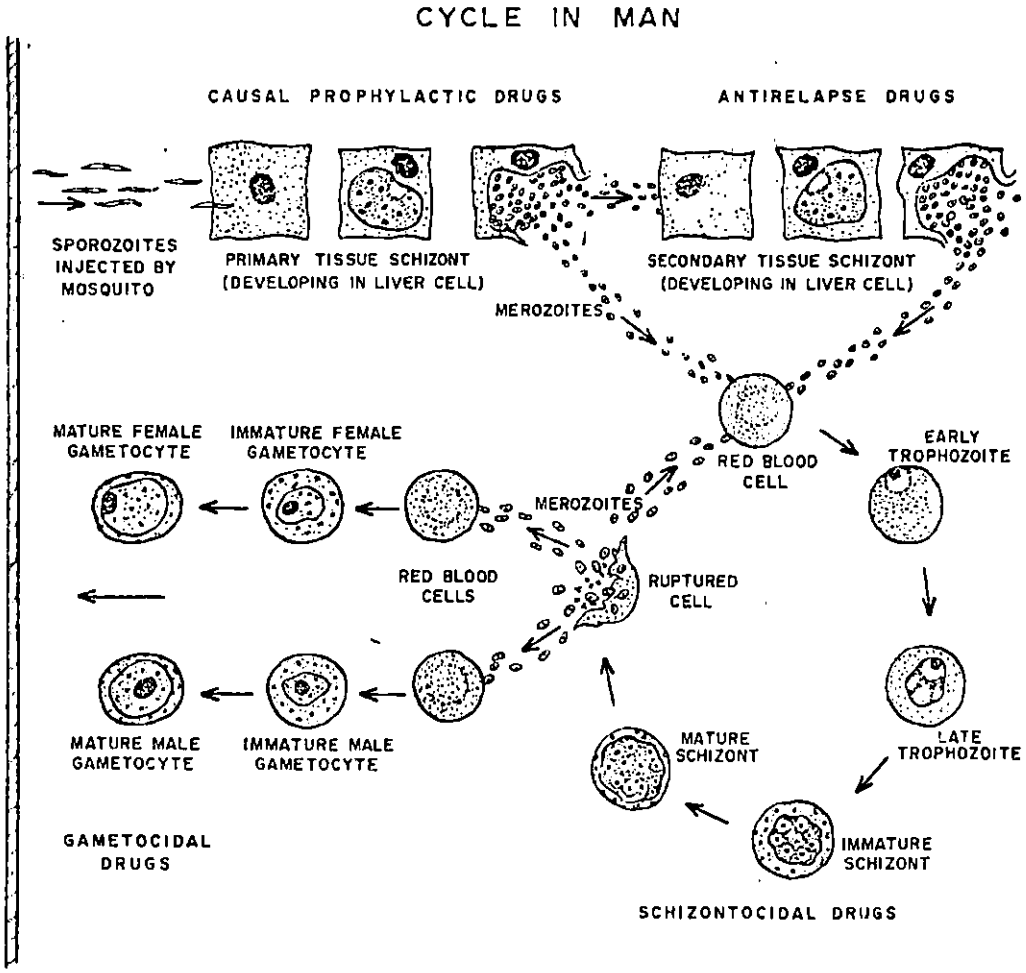


Figure 1 (Continued)

2. Extrinsic cycle (sexual generation)

An Anopheles mosquito bites an infected person. Gametocytes are contained in the blood meal, which is held in the mosquito's stomach for digestion. Once in the stomach, the gametocytes mature into "respective" male and female gametes. A male and female gamete fuse producing a zygote. After elongation and becoming motile, the zygote, now designated as an "ookinete", moves to the stomach wall, penetrates it and forces until it rests between the outer membrane and the inner epithelial cells. Then the ookinete develops as an oocyst. The oocyst increases in size, due to the numerous sporozoites developing within it. Finally, the oocyst ruptures, releasing the sporozoites into the mosquito's body cavity. Once released, the sporozoites migrate to the salivary glands where they are released with salivary secretions (some of which are anticoagulants), at the next blood meal. The duration of the extrinsic cycle is temperature dependent. This has much epidemiologic significance, as will be shown in Table 1 (Garnham, 1966).

3. The clinical disease

There are no obvious symptoms displayed by a host, while the parasite is in the liver. After an "incubation" period, the schizonts release billions of merozoites simultaneously into the bloodstream. Clinical symptoms then appear. Parasitaemaia becomes patent and cycles of chills, fever and sweating occur. These cycles are believed to

Table 1. Information on species of Plasmodium infective to humans (Garnham, 1966)

Species of Plasmodium	Location	Clinical disease in man	Sporozoite development
P. vivax[a] (most common)	world-wide distribution, flourishes best in temperature climates	rarely fatal disease, uses young rbc's	9 days at 24-25C 16 days at 20C
P. falciparium[b]	thrives best in hot climates, mainly confined to the tropics and subtropics, can be found in temperate zones	most lethal form, often fatal if not treated	10 days at 25C 23 days at 20C
P. malariae[c]	spotty, found in tropics and temperate zones	mild, tenacious fever, uses aging rbc's	15-20 days at 25C
P. ovale[d]	found in tropics and sub-tropics, irregular	mild infection of short duration	14 days at 27C

[a] P. vivax has the ability to withstand therapy, remains chronic, causing severe anaemia.

[b] P. falciparium multiplies and interferes with blood flow, blocking capillaries and passages, at 40-55 days sporozoites become noninfectous, less common in people with sickle cells.

[c] P. malariae develops with difficulty in mosquitoes, persists because remains latent in blood for years and then shows up much later, has been known to infect chimpanzee.

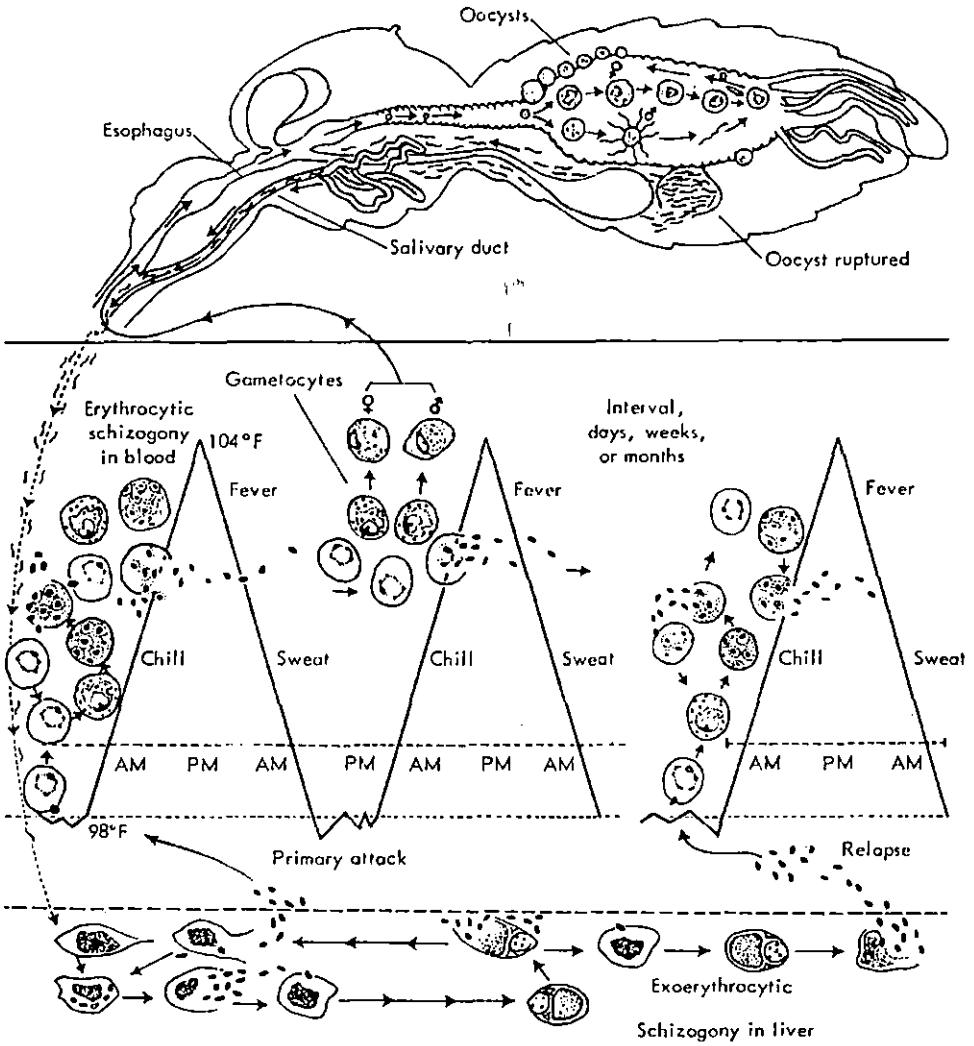
[d] P. ovale tendency for prolonged latency before attack.

be caused by the release of a toxin along with the merozoites (Jones, 1967). Notice the relationship between temperature change and merozoite release (Figure 2). The loss of numerous rbc's due to merozoite invasion, may cause anemia if sufficiently massive. Plasmodial infection leaves the victim typically in a weakened state and predisposed to other infections. Some cases become chronic (Jones, 1967).

B. Epidemiology: The Important Factors in Malaria Distribution

The geographic distribution of human malaria is limited by several factors. It requires certain species of Anopheles, man and a suitable environment for transmission. Suitable environment for transmission means suitable habitat for man and mosquitoes at a suitable temperature for parasite development. The different plasmodia need different temperatures for optimum development in the mosquito (see Table 1 for specifics). These temperatures restrict malaria to the tropic, subtropics and temperate zones. Another requirement for transmission is contact between mosquito and available gametocyte carriers. And later, contact between mosquitoes and a susceptible human population.

For wide geographic malaria distribution, the mosquito must be an "efficient" vector. Efficient mosquito vector populations depend on suitable environmental conditions. The mosquito larvae are aquatic and they require water.



Life cycle of *Plasmodium vivax*. Gametocytes are taken with blood into the mosquito's stomach, where fertilization occurs. Oocysts form in the wall of the stomach and liberate sporozoites which invade the salivary gland. When injected into a human host, the sporozoites enter liver cells, where several cycles of schizogony occur, resulting after some days or weeks in a primary attack of malaria. Synchronized at 48-hour intervals, the attack is characterized by schizogonic cycles in the blood. The cycles include chills, fever, sweating, and eventual recovery. After an interval varying from days to months, relapse may occur because of the continued presence of exoerythrocytic stages in the liver. Relapse is characterized by the same symptoms and blood forms as were seen in the primary attack.

Figure 2. The clinical disease (Jones, 1967)

Water may be an irrigation ditch, a pond, a puddle, or even a hoofprint filled with water. The different species flourish in different habitats. Some prefer shade, some prefer sunshine. Any change in the environment may alienate one species and encourage another.

1. The vector

There are 3100 known species of mosquitoes (Culicidae) in the world today (Knight and Stone, 1977). More species are continually being identified as taxonomic difficulties are resolved. A total of 401 species and subspecies have been described in the genus, Anopheles (White, 1979). Of these, more than 80 species of Anopheles are known to be involved as vectors for the malaria parasite in man (White, 1979). "Only about 60 species, however, are sufficiently closely associated with man to rank as important vectors, or carriers of disease. Generally, a continent or group of countries has no more than 10 different species of Anopheles that act as vectors, and often no more than one or two species are the main transmitters of malaria" (Alvarado and Bruce-Chwatt, 1962).

The Anopheles mosquito is the known vector of human malaria (White, 1979). Transmission will depend on the species and the choice of meals available. Species demonstrate different feeding preferences. A mosquito's preference for human blood is recorded as the "human blood

index", earlier known as the "anthropophilic index." The human blood index is dependent upon the species considered, the area collected, and the sampling occasion (Garrett-Jones, 1964).

a. Life cycle of the mosquito The eggs are deposited singly or in batches (depending on the species) by a female mosquito in water or in a spot where water will reach later. Once the egg is in the water, it hatches and a larva emerges. The larva's main function is to eat and grow. It feeds on organic debris in the water. It requires atmospheric oxygen for respiration (Daly et al., 1978). Complete metamorphosis occurs and the adult mosquito emerges.

b. Adult males The adult male mosquito does not feed on blood; instead, it lives on various plant juices. Its primary function is to fertilize the female. Because the male mosquito plays no direct role in transmission of Plasmodium, it will not be discussed further.

c. Adult females An adult female mosquito requires blood, with its quantities of protein, for the production of fertile eggs. "A normal mosquito meal (of human blood), would consist of from forty to fifty million cells, anyone of which, it will be recalled, might contain another whole

animal, plasmodium" (Harrison, 1978). While the mosquito is sucking up blood, it releases saliva, with its anti-coagulants in little bursts.

The adult female can become inseminated after 24 to 48 hours of emergence (White, 1979). After copulation, the sperm pass into the spermathecae, a storage organ for sperm. At each ovulation, some of the sperm are released to fertilize the eggs as they pass on their way out of the oviduct. Usually, there are enough sperm furnished with one mating to fertilize the eggs for the lifetime of the mosquito, making it unnecessary to mate a second time.

For each blood meal, one brood of eggs will develop. The size, color and formation of the brood depends on the species and the environment.

d. Potential A mosquito has tremendous reproductive potential. It can produce a large number of offspring in a short time. Because of this potential it is difficult to destroy any mosquito population by diminution of sheer numbers, without a thorough, intensive and complete attack. This was demonstrated during the construction of the Panama Canal.

Mosquitoes are also very adaptable insects. They are small in size and cryptic. The mosquitoes generation time is short. They can adapt easily to a changing

environment, sometimes with concomitant genetic changes. For this reason, some mosquito species have evolved a high order of resistance to pesticides.

2. Immunity in man

After an acute attack of malaria, the human body may develop a partial immunity. This immunity is temporary, low level and specific to the plasmodium strain. It will continue for the length of time that the few remaining parasites in the blood stimulate the immune system (Garnham, 1966). After repeated, chronic infections a higher level of immunity may result. The higher level of immunity is evident by fewer and milder clinical symptoms from an infection; parasitaemia and gametocytaemia become suppressed. This, too, is of great epidemiological significance.

C. Modeling

1. History

Progress in modeling epidemic diseases started in the 19th century. Before this time, required mathematical techniques were developing along with a precise hypothesis for disease. The models were proposed to help clarify existing biological concepts and to aid in the explanation of major observable phenomena. The first modeling began with curve-fitting data and then predicting from the curve.

Table 2. History of malarial advancement (Garnham, 1966)

400 BC	Hippocrates, "the father of medicine", studied in Egypt first malariolist; he recognized and clinically described fevers
	Later Greek and medieval physicians did little to advance knowledge
1717	Lancisi - origin of diseases, and insect arising from marshes (i.e., a relation between marsh and occurrence of malaria)
1775	Torti - all fevers are not malarial, quinine only effective on malarial infection; diagnostic tool
1820	Pelletier and Caventou - 2 French chemists isolated the active principle from quinine
1831	Boyle - swamp theory: ". . . heat and moisture combine to excite the deadly principles of malaria, which are wafted in the early morning like smoke or steam over the streets of the nearby town to infect the inhabitants"
1880	Lavern noted strange forms in the blood; observed exflagellation malaria - a parasite in the blood
1897	Maccallum - discovered sexual nature, deduced male and female parasites; observed fertilization
1898	Ross, an Englishman, observed sporogonic cycle in avian malaria and transmission to healthy sparrows
1898	Bignami, Italian, infected a human volunteer with P. falciparium; Grassi, Italian, infected subject with Anopheles; demonstrated complete malaria cycle
1911	First malarial mathematical model offered by Ross
1926	James and Shute - large scale treatment of syphilis with malaria, good opportunities for human research on malaria
1948	Short and collaborators demonstrated incubation stage, or erythrocytic cycle in liver of humans

In 1911, Ross presented the next step in modeling. He designed a structured mathematical model for malaria using a set of basic parameters. His model was the first to use a well-organized mathematical theory as a research tool in epidemiology (Bailey, 1975).

The more significant attempts to model malaria are covered in Chapter 17 of Bailey's "The Mathematical Theory of Infectious Diseases". For a discussion of these models, the reader should refer to Bailey. These models attempt to deal with the human population, while considering immunity, superinfection and seasonal variations.

2. Inoculation rate

To compare the levels of intensity of malaria between different areas, several indices were used to help evaluate the malaria transmission between people and mosquitoes (Swaroop, 1966). One important index is the inoculation rate. The inoculation rate is the proportion of a population receiving infective inocula in one day (i.e., the risk of infection for an individual, assuming homogeneity of risk over the subject population). This rate can be estimated in the field in two ways; one method is by a parasitological survey of the human population and the other by entomological measurements (Swaroop, 1966). To estimate the inoculation rate by parasitological means, the parasite rate is measured

in children of two years or younger, because they may not have developed an immunity (Macdonald, 1950). The entomological approach estimates the density of infective Anopheles, relative to man. This requires the measurement of the sporozoite rate (s), the estimation of the number of bites by Anopheles per individual per day (ma), and the measurement of the number of these bites that are infective (b). The entomological inoculation rate is equal to the product of (ma)(s)(b) (Macdonald, 1952).

3. Macdonald's sporozoite rate

"It (sporozoite rate) is very commonly measured in field survey and the direct object of malaria control by imagocides is its reduction to negligible levels. Though there have been mathematical working on its constitution it is curious that there is no generally accepted basis of theory or observation relating it to the factors on which it depends, and showing how it would be expected to vary with changes in these factors . . . the immediate object of the present study (Macdonald's) is to create such a theory. The factors affecting the rate are first considered and they are then brought together into a general relation expressed as a formula" (Macdonald, 1952).

Before developing Macdonald's formula for sporozoite rate, first it is necessary to define symbols and state basic

assumptions for the model. The symbols are defined by Macdonald (1952) as follows:

a = the average number of blood meals on man taken by a mosquito in a day

p = the probability that a mosquito will survive through one day

n = the time in days taken for the completion of the extrinsic cycle (of the parasite) in the mosquito

x = the proportion of bites on man which are infective to the mosquito (1952); the proportion of the people affected (1957)

s = the proportion of mosquitoes with sporozoites in their salivary glands

Macdonald made several assumptions for the sporozoite model. He considered the case of stable malaria, where the prevalent state of malaria is one of equilibrium. The mosquito and human population are assumed constant, with the number of births equalling the number of deaths and with generations that constantly overlap and with a migration that is negligible. The human population provides a constant source of infection for the mosquito and the mosquitoes feed randomly among the people. The contacts between the mosquitoes and infectious people (ax) are normally distributed (Poisson) (Muench, 1959).

Mosquitoes once infected with sporozoites are considered to remain infected for their lifetimes (Macdonald, 1973). There are cases where this assumption was found to be incorrect. The probability of survival through one day

for a mosquito is considered a constant. Macdonald (1952) reasoned that the daily hazards of life should fall equally on all mosquitoes regardless of age, and also a mosquito should not die of degenerative causes until two or three months of age.

Macdonald developed his formula for the sporozoite rate algebraically. Dr. Armitage published the same formula about a year later using calculus. His development allowed for a continuous function with respect to time. This is the development I will review.

"Infection Rate in Mosquitoes"

Suppose the probability of a mosquito surviving t days is e^{-vt}, so that, in Macdonald's notation, $p = e^{-v}$ and $v = -\log_e p$. Assuming that the mosquito population is stationary, births being balanced by deaths, the proportion of mosquitoes alive at any moment which were born between t and t+dt days ago is

$$ve^{-vt}dt \; . \qquad (1)$$

Let n be the length of the extrinsic cycle, a the mean number of men bitten be one mosquito in a day, and x the proportion of people infected. Then, for t>n, a mosquito aged t days will have had t-n days on which it might have fed on human beings, in order to be infective by the present time. The probability that in an interval of t-n days a mosquito bites at least one infected person is

$$1-e^{-ax(t-n)} \; . \qquad (2)$$

The proportion of infected mosquitoes is, therefore, from (1) and (2),

$$s = \int_n^\infty ve^{-vt}(1-e^{-ax(t-n)})dt = \frac{axe^{-vn}}{ax+v}$$

$$= \frac{p^n ax}{ax-\log_e p} . \qquad (3)$$

This expression for the infection rate in mosquitoes is the same as that derived by Macdonald (1952) by a rather different method. In both derivations a constant value of x is assumed, but it would be reasonable to use this formula for s even if x were changing moderately, using the value of x which prevailed rather more than n days before (Armitage, 1953).

There are other possible points of variation to consider also. The Anopheles species vary among themselves. Certain species may be more susceptible to different strains of parasites (Garnham, 1966). The Anopheles blood meal preference, i.e., the anthropophilic index, depends on the local situation and the relative availability of different hosts. Ambient temperature will strongly affect the value for n, and the minimum number of days necessary for extrinsic development before a mosquito is infective. These points can affect the overall value of s for any particular Anopheles species.

Despite its ambiguity, the formula for the sporozoite

rate is a valuable tool to have. It shows the relative importance of each factor and how they fit together to form the sporozoite rate, which is a sizable influence in determining malaria incidence (Macdonald, 1952). Field estimates can be obtained for s, n, a, and p. Then, with the help of the sporozoite formula, a value for x can be estimated, because it is not easily measured by itself. The value for x, when calculated using the sporozoite model shows a fair degree of correspondence with the value of x obtained by another method according to the experimental results of Davidson and Draper, 1953. Further comparisons between the sporozoite calculated x, and other values of x for an area showed that the calculated x may not represent the actual situation (Garrett-Jones and Shidrawi, 1969). Another indication of lack of precision in the sporozoite rate model is pointed out in estimates of Anopheles survival rate. Gillies and Wilkes (1965), demonstrated a lack of agreement between measured results and calculated estimates from the epidemiological analysis of the sporozoite rate.

In this work, Macdonald's "sporozoite rate" model will be examined, beginning with an investigation of the assumptions of the model. Next, the possibility that mortality risk may increase with vector age is explored, as was suggested by Gillies' and Wilkes' data. If this is so,

then, can Gillies' and Wilkes' date be modeled in a form that can be usefully incorporated into Macdonald's formula?

II. METHODS AND ANALYSIS

A. Justification for Macdonald's Model

We can derive Macdonald's model by another means. Begin by assuming that the death rate of an insect population can be modelled according to what is termed a Poisson process. A Poisson process explains the generation of discrete events (deaths) in a continuous interval (time). It is based on two assumptions; first, in a short time interval of length, h, the probability for one occurrence (death) is approximately vh, where v describes the intensity of the process, i.e., a larger value of v indicates more deaths, and a smaller value of v indicates fewer deaths. The probability of two or more occurrences is negligible; secondly, we assume that events are mutually independent. That is, the occurrence of any one event in an interval has no effect on and is not affected by the occurrence of an event in another interval.

A Poisson process, with intensity parameter v, can describe the probability that k events occur in the time period (0,q) by

$$P\ (k \text{ events in the time period } (0,q)) = \frac{(vq)^k e^{-vq}}{k!}$$

v = intensity/time

k = number of events; = 0,1,2,...

q = units of time (Larson, 1974).

For the case of the death of an insect, let p equal the probability of survival for one day, that is the probability of zero deaths for one day. Then, k = 0, q = 1 day and p = P (0 deaths in 1 day) = e^{-v}. Macdonald assumed that the probability of surviving one day was a constant, e^{-v}.

Given that the probability of surviving for one day is a constant, e^{-v}, then the probability of surviving for t days is e^{-vt}. This can be demonstrated using conditional probability.

$$P(\text{surviving } t \text{ days}) = P\left(\text{surviving from } t\text{-}1 \text{ to } t \,/\, \text{alive at } t\text{-}1\right) \times P(\text{surviving } t\text{-}1 \text{ days})$$

$$= e^{-v} \times P\left(\text{surviving from } t\text{-}2 \text{ to } t\text{-}1 \,/\, \text{alive at } t\text{-}2\right) \times P(\text{surviving } t\text{-}2 \text{ days})$$

$$\vdots$$

$$= (e^{-v}) \times (e^{-v}) \times (e^{-v}) \ldots P\left(\text{surviving from 0 to 1 days} \,/\, \text{alive at } t=0\right) \times P(\text{alive at } t=0)$$

$$= \prod_{n=0}^{n=t} e^{-v} = e^{-vt}.$$

This can also be based on the assumption of a negative exponential survival curve (Bailey, 1975 and Gross and Clark, 1975).

Once the survival curve S(t) is determined, the death density function f(t) can be obtained; $f(t) = -S'(t)$. This can be used to determine the proportion of mosquitoes alive between the time t and t+dt, $(ve^{-vt}dt)$.

Proof: The probability of living from day 0 to day t = e^{-vt}

The probability of living from day t to $+\infty$ $1 - e^{-vt}$

Determine the proportion of mosquitoes alive between time t and t + dt.

$$\lim_{dt \to 0} \frac{(1-e^{-vt}) - (1-e^{-v(t+dt)})}{dt}$$

$$= (1-S(t))' = -S'(t) = ve^{-vt}dt$$

Next, we determine the probability of at least one infective feed. Consider a feed to be infective or non-infective. Then, we use the Poisson process to model the probability of an infective feed. If we define an event to be an infective feed, then the probability of no infective feeds, equals;

$$P(0) = \frac{(vq)^0 e^{-vq}}{0!} = e^{-vq} = e^{-ax(t-n)}$$

v = intensity/time = ax

q = units of time

(t-n) = the length of time infective.

Then, the probability of at least one infective feed is equal to one minus the probability of zero infective feeds;

$1 - e^{-ax(t-n)}$.

The proportion of infected mosquitoes (s) is equivalent to the probability of an infective bite times the proportion of mosquitoes alive at any moment. We use n as a lower limit as this is the zero time for the mosquito to become infectious. Therefore,

$$s = \int_n^\infty ve^{-vt}(1-e^{-ax(t-n)})dt$$

$$= \frac{axe^{-vn}}{ax+v}$$

Since $p = e^{-v}$, $v = -\log_e p$; by substitution

$$s = \frac{axp^n}{ax-\log_e p}.$$

This is the same model as derived by Macdonald (1952). The variables a and p are intrinsic to the mosquito population, while x and n are extrinsic to the mosquito population. x is intrinsic to the human population and n is intrinsic to the environment and the strain of parasite.

B. Influences on s

To further investigate Macdonald's model, we examine how each term will influence the value of s, the sporozoite rate. This can be done by scrutinizing the first and second derivatives of s with respect to each variable, while holding the other terms constant. The first derivative defines the slope of the line. Using s as a function of each variable, a positive first derivative would indicate that the value of s increases with the increasing value of the variable. A negative value for the first derivative results in the value of s decreasing with the increasing value for the variable. The second derivative indicates the type of concavity, that is, whether the rate of change is increasing or decreasing. A negative value indicates that it will take increasing amounts of the variable for each equivalent amount of increase in s to occur. A positive value can be interpreted as requiring a smaller change in the variable to create each successive equivalent increase in s. Then, the second derivatives can be compared to determine which variable has the largest effect on the value of s, i.e., which rate of change increases most rapidly.

As stated in the introduction, the calculated value of s and the measured value for s do not agree. The possibility that this is due to the choice of the wrong survival curve

will be examined using data from Gillies and Wilkes (1965). The first question is whether Macdonald's choice of a simple exponential survival distribution closely models the data. Secondly, we examine presumptive mortality, i.e., the mortality rate per age interval, to see if it models the data. Then, if the survival distribution and the presumptive mortality indicate that another model may fit better than an exponential, we attempt to define this model.

C. Gillies and Wilkes Paper

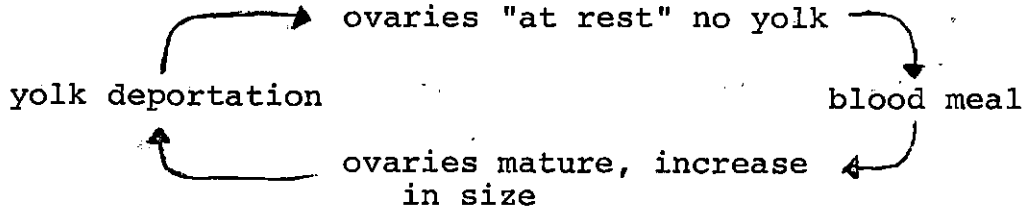
The paper by Gillies and Wilkes (1965) is a study of the age composition of natural mosquito populations. Female mosquitoes are aged by counting the dilatations on the ovarioles. One dilatation indicates 1-parous, two dilatations, 2-parous and so on. The determination of the exact age of older mosquitoes cannot be considered highly accurate, because of degeneration of follicles and because not every ovariole participates in each cycle. To help relate physiological age to calendar age, laboratory-reared females of A. gambiae were marked and released at Muheza. The numbers recaptured were recorded. Thirty-two out of sixty were nulliparous or pregravid. After plotting the recaptured data, they found it took three to four days for the first gonotrophic cycle and approximately three days each for the later cycles.

The sampling of mosquitoes was from November 1962, to January 1964, in two areas of Tanzania. A. gambiae and A. funestus populations were sampled at Muhuza and A. gambiae at Gonja. A. gambiae was found to be an homogenous population at Muheza. However, the A. gambiae population at Gonja had species A and B present. The area had an average temperature ranging from 73°F in July to 81.5°F in March. There was an average rainfall of 50 inches, and a high humidity year-round.

The data collected are in three main development groups, pregravid, nulliparous and parous (Table 3). The pregravid and nulliparous groups require evaluation to

Table 3. Age groups of mosquitoes

pregravids	first, partial blood meal (day 1 or 2 of age)
nulliparous	never laid eggs (day 0-5)
parous	laid one or more batches of eggs (days 6-∞)
gravid	bearing mature, ready to lay, eggs (a portion of the "gonotrophic cycle")



temperature dependent process, 2-3 days between oviposition

determine if they are significantly different from the parous group. Gillies and Wilkes excluded the pregravid group because it consisted of freshly-fed females only. It is unlike the other age groups, which have two or three stages - fed, halfgravid, or gravid. Therefore, it does not represent a comparable sample. Also, the interval between the first and second blood meals is only one or two days, while all the other later feeds are three days apart. Again, this will affect the sample. The decision to not include the pregravid group will be followed in this work.

They also evaluated the nulliparous group and found more nulliparous A. funestus resting indoors by day than were caught biting indoors at night. It was concluded that nulliparous females have a greater tendency to leave after feeding than do parous females. Records of parous rate for A. gambiae at Kihurio in the Pare district, sampled indoors and out, indicate that significantly more nulliparous females rest indoors than out. Detinova (1962) found good evidence that a high proportion of nulliparous females rest outside, so that house catches are not a proper representation. Hamon, Chauvet and Thélin (1961), and Gruchet (1962), found nulliparous females of both A. gambiae and A. funestus to be more common in outdoor resting sites. The results are too conflicting to establish a comprehensive picture of the resting habits of nulliparous females. Therefore, they will

be disregarded in analysis.

D. Weighted or Unweighted Results

The age composition for A. gambiae at Gonja was statistically stable as were the A. funestus and A. gambiae populations at Muheza (Table 4). The slight difference at Gonja was due mainly to a lower fraction of pregravids in housecatches in the dry season. This is possibly due to seasonal changes in resting habits.

Table 4. Age composition

	1-parous and younger	3-parous and older
A. gambiae at Gonja		
hot (wet) season	72.7%	11.5%
cool (dry) season	67.2%	16.3%
A. gambiae at Muheza		
hot (wet) season	63.0%	22.7%
cool (dry) season	64.0%	20.0%
A. funestus at Muheza		
hot season (Nov.-April)	58.7%	24.2%
cool season (May-Oct.)	58.8%	23.1%

The age composition is a result of the total of collections of the population over a period of time. Assuming each month to be of equal value in determining the overall age composition, then ideally every month the same number

of A. gambiae and A. funestus would be collected; unfortunately this is not the case. The population size (or numerical count) changes with the different seasons from large to small to large, and so forth. It was noted, however, that the changes in age composition were slight; that is, the proportion in the population did not change, only the numbers.

Gillies and Wilkes used weighted values for the age composition because the numbers of mosquitoes caught per month varied with the different months of a year. Two hundred or more females were dissected each month, except when that number could not be caught. Some months the numbers of mosquitoes were so large that it was impossible to dissect all the mosquitoes collected. As many as possible were dissected. To determine if the error in the weighted case is larger than the error in the unweighted case, we begin with a set of trial data (Table 5).

Table 5. Trial set of data

		Number dissected	Percent of catch dissected
Total catch abundance/ half month	1000	500	50%
	800	425	53
	500	400	80
	300	300	100
	200	200	100
	180	180	100

Assume each dissected group has a set amount of error, 5%. Then, calculate the proportion of the total that each age group is; i.e., $P_{ij} = \frac{\#\ i^{th}\ \text{age group}}{\#\ \text{dissected in catch}}$, where i is the age group and j is the catch.

$$\text{To calculate weighted \# for the age group} = \frac{P_{i1}\bar{C}_1 + P_{i2}\bar{C}_2 + P_{i3}\bar{C}_3 + \ldots + P_{i26}\bar{C}_{26}}{26}$$

where $\bar{C}_k$ = total catch abundance/# houses; k = 1 to 26. Given that P_{ik} has a 5% error, to multiply it by C_k will magnify this error if the number dissected is less than the total caught. Example: the number caught is 1000, the number dissected is 500; therefore, the proportion dissected is equal to 50 percent; $P_{ij}C_k$ has an error of five percent times two or a ten percent error. Error magnification is smaller when the proportion of catch is large. The number calculated for each age group cannot be more precise than the least precise of its terms, that is to say, if one term has ten percent error and the other terms less than ten percent error, then the answer itself will have at least ten percent error. Compare this with the unweighted case, wehre again P_{ij} is calculated. The number for an age group is computed as:

$$\#\ \text{for age group} = \frac{P_{i1}n_1 + P_{i2}n_2 + \ldots + P_{i26}n_{26}}{n_1 + n_2 + \ldots n_{26}},$$

where n_k is equal to the total number of dissected mosquitoes.

The error term is not magnified, so it is equal to 5 percent. In this work the unweighted data were used, because they should have the least amount of error.

Another question to address is, how significant is the fact that the number of mosquitoes collected in some months is too large to dissect completely? Assuming the number sampled is greater than or equal to two hundred, then we can apply the central limit theorem. It states; "If n is large, then $\frac{\bar{x} - \mu}{\lambda/\sqrt{n}}$ has approximately a standard normal distribution, or $\bar{x}$ has approximately a normal distribution with mean and standard deviation $\sigma/\sqrt{n}$" (Ott, 1977).

Since there was no significant change in age composition, it will be assumed that the population was in equilibrium. Therefore, sampling continuously for a length of time, despite changes in the sample size, shall be considered a fiar representative sample method where no weighting is needed.

E. Determining a Better Model for the Survival Curve

1. Life table evaluation

Life tables are one way of expressing a quantitative description of some particular population during some chosen period of time. They present the data in a form that is convenient for comparison between populations and times. A time-specific life table can be used if it is justified

to assume a steady population (Southwood, 1978).

The time-specific life table consists of seven columns. They are defined by Southwood (1978) and Gross and Clark (1975), as follows:

1) z - Age interval, the period of life between 2 exact ages z is the center of the interval, in this case z = the number of oviposition

2) l(z) - the number of individuals surviving at the beginning of the age interval, i.e., the number collected of age z

3) d(z) - the number dying during the age interval (l(z) - l(z+1))

4) L(z) - number alive between z and z+1 = $\frac{l(z) + l(z+1)}{2}$

5) T(z) - number alive in this and all subsequent intervals = $\sum_{t=0}^{z} L(z)$

6) e(z) - the expectation of life, remaining for individuals of age z = $\frac{T(z)}{l(z)}$

7) q(z) - the mortality rate per age interval, presumptive mortality, i.e., the proportion dying = $\frac{d(z)}{l(z)}$.

A time-specific life table presents the age structure of a population at a point in time. Table 6 is a time-specific life table for the simulated population distribution of Macdonald, where $N(t) = N_o e^{-vt}$. Tables 7, 8 and 9 are time-specific life tables for the three different populations in Gillies' and

Table 6. Simulated population: $N(t) = N_o e^{-vt}$, $v = .5$

z	l(z)	%S(z)	d(z)	L(z)	T(z)	e(z)	q(z)
1	1000.00	100.00	393.47	803.26	2044.19	2.044	.393
2	606.53	60.65	238.65	487.20	1240.93	2.046	.393
3	367.88	36.79	134.75	300.50	753.73	2.049	.366
4	233.13	23.31	97.80	184.23	453.23	1.944	.419
5	135.33	13.53	53.25	108.70	269.00	1.988	.393
6	82.08	8.21	32.29	64.94	160.30	1.953	.393
7	49.79	4.98	19.59	40.00	95.36	1.915	.393
8	30.20	3.02	11.89	24.26	55.36	1.833	.394
9	18.31	1.83	7.20	14.71	31.10	1.699	.393
10	11.11	1.11	4.37	8.93	16.39	1.475	.393
11	6.74	.67	2.65	5.42	7.46	1.107	.393
12	4.09	.41	-	2.04	2.04	-	-

Table 7. A. gambiae at Gonja

z	l(z)	%S(z)	d(z)	L(z)	T(z)	e(z)	q(z)
1	766	100.00	35.51	82.24	170.21	1.702	.355
2	494	64.94	33.94	47.52	87.97	1.364	.526
3	234	30.55	13.97	23.56	40.45	1.324	.457
4	127	16.58	10.80	11.29	16.89	1.019	.651
5	46	6.00	3.91	4.04	5.60	.933	.652
6	16	2.09	1.70	1.24	1.56	.746	.813
7	3	.39	.26	.26	.32	.820	.667
8	1	.13	.13	.06	.06	.461	1.00

Table 8. A. funestus at Muheza

z	l(z)	%S(z)	d(z)	L(z)	T(z)	e(z)	q(z)
1	815	100.00	14.36	92.82	249.41	2.494	.144
2	698	85.64	33.98	68.65	156.59	1.828	.397
3	421	51.66	18.65	42.34	87.94	1.702	.361
4	269	33.01	16.81	24.61	45.60	1.381	.509
5	132	16.20	7.87	12.27	20.99	1.296	.486
6	68	8.34	5.89	5.40	8.72	1.046	.706
7	20	2.45	1.22	1.84	3.32	1.355	.498
8	10	1.23	.49	.99	1.48	1.203	.398
9	6	.74	.62	.43	.49	.662	.838
10	1	.12	.12	.06	.06	.50	1.00

Table 9. A. gambiae at Muheza

z	l(z)	%S(z)	d(z)	L(z)	T(z)	e(z)	q(z)
1	804	100.00	33.09	83.46	215.94	2.159	.331
2	538	66.91	26.86	53.48	132.48	1.980	.401
3	322	40.05	13.56	33.27	79.00	1.972	.338
4	213	26.49	10.20	21.39	45.73	1.726	.385
5	131	16.29	5.59	13.50	24.34	1.494	.343
6	86	10.70	7.59	6.91	10.84	1.013	.709
7	25	3.11	2.11	2.06	3.93	1.26	.678
8	8	1.00	.25	.88	1.87	1.87	.250
9	6	.75	.50	.50	.99	1.32	.667
10	2	.25	0	.25	.49	1.96	-
11	2	.25	.13	.18	.24	.96	.520
12	1	.12	.12	.06	.06	.50	1.00

Wilkes' paper. Also added to the tables is S(z), a normalized l(z), $(\frac{l(z)}{l(0)})$, so that the percentage in each age group for the different survival distributions can be compared without equal numbers. For comparison, %S(z), the expected life, e(z), and presumptive mortality, q(z), have been graphed versus the number of ovipositions. Graphs of e(z) and q(z) are used to check the fit of the model for S(z).

If $\%S(z) = e^{-vz}$ is plotted on semilog paper, it should yield a straight line, as shown in Figure 3. Semilog plots of %S(z) from Gillies' and Wilkes' data are shown in Figures 5, 6 and 7. The data can be modeled by a straight line. However, the values for six parous and older age groups fall below the line. The older age groups are important to consider in the sporozoite rate, because a mosquito can be infectious only after n days. Consider an average value for n to be equal to 4 or 5 parous. Graphically, the %S(z) semilog plots suggest that the data may be better modeled. Next, examine the expectation of life plot, e(z), for a simple exponential, $S(z) = e^{-vz}$, as shown in Figure 4. The value for e(z) remains constant for the younger age groups and then gradually drops with increasing age. Plots of e(z) for the three populations (Figures 8, 9, 10) from Gillies' and Wilkes' data have a decidedly linear trend. The plot in Figure 4 of presumptive mortality q(z) for the $S(z) = e^{-vz}$ case,

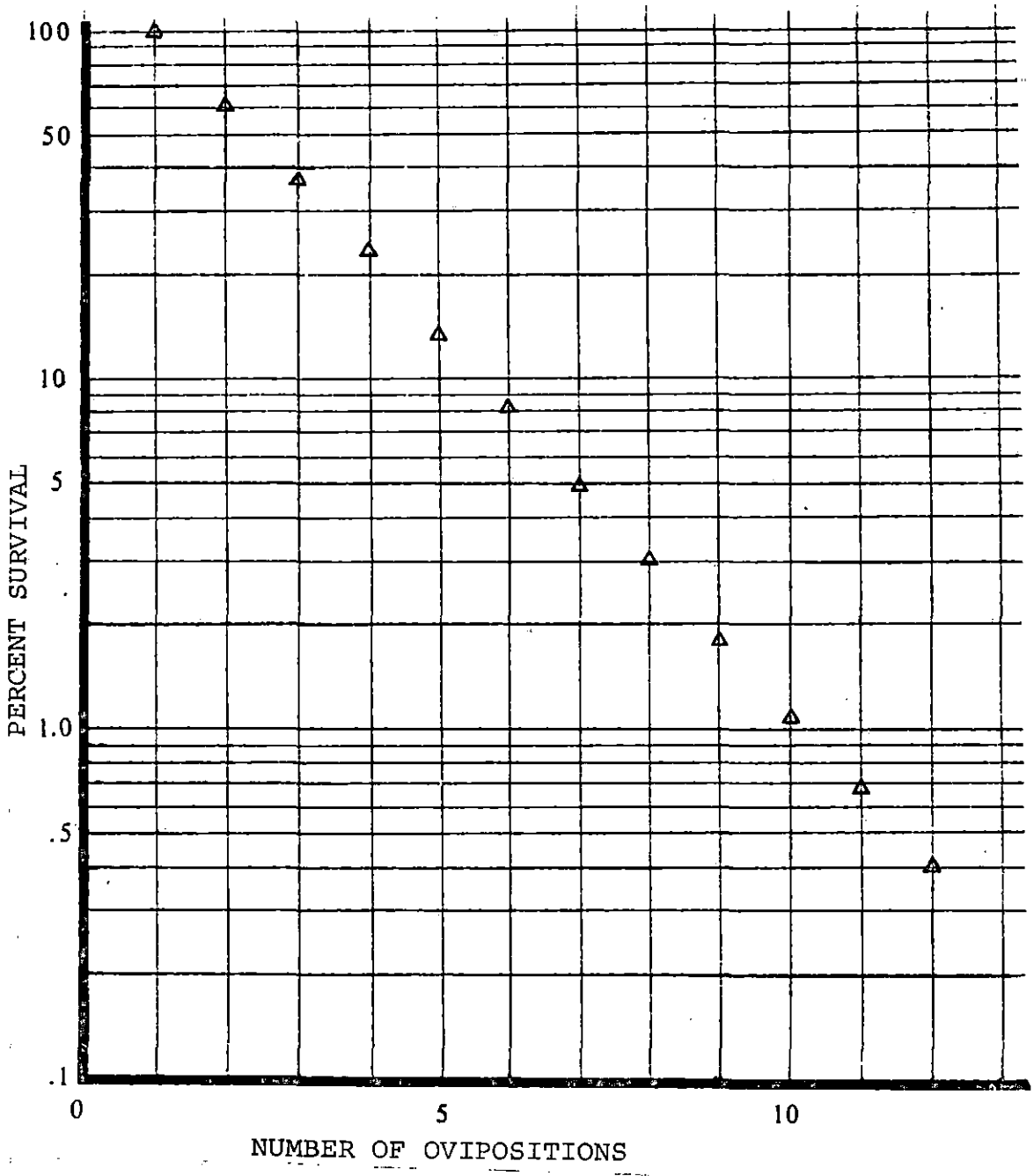


Figure 3. Simulated population for Macdonald's model, percent survival versus the number of ovipositions

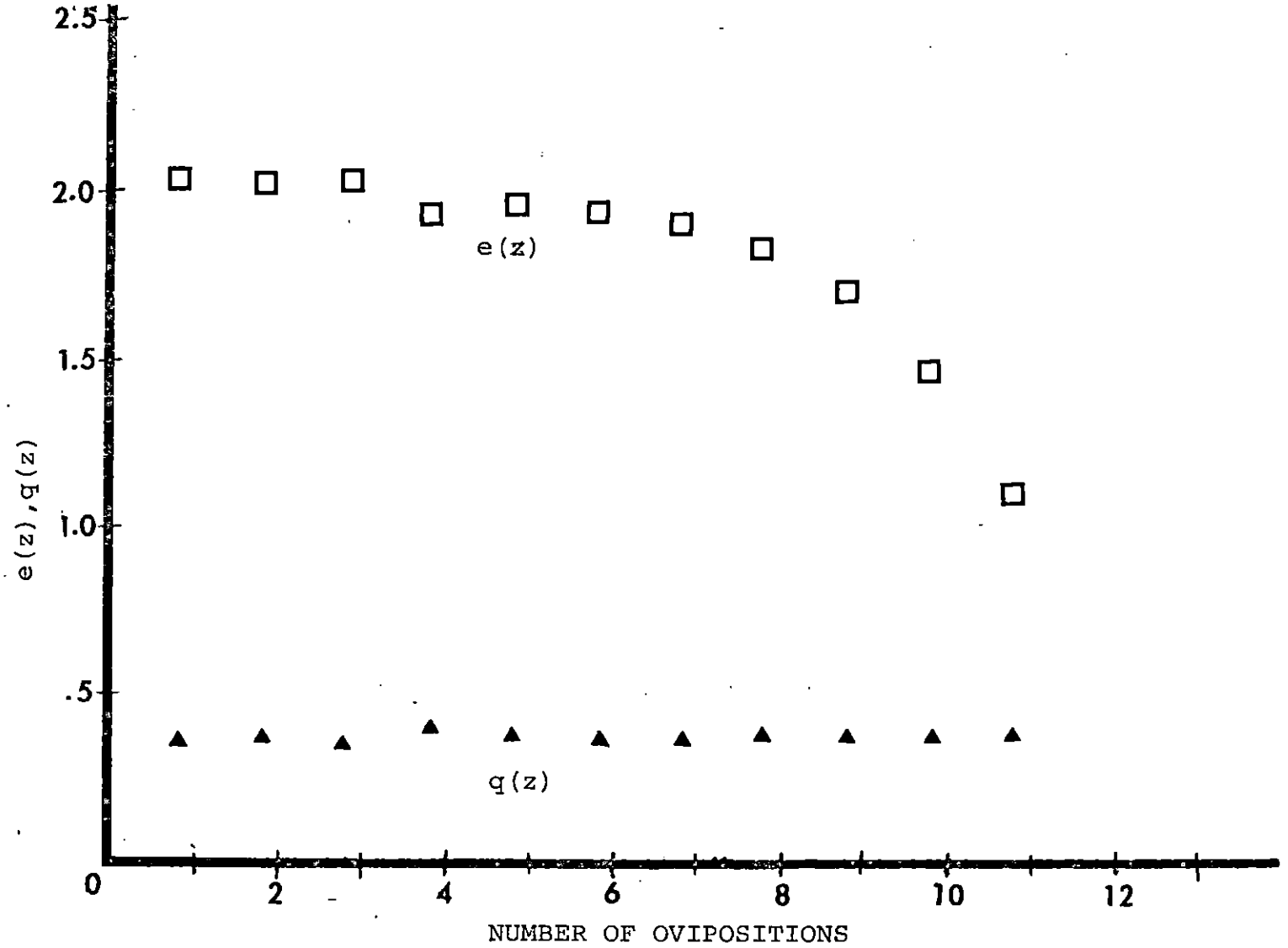


Figure 4. Simulated population for Macdonald's Model, expected life e(z) and presumptive mortality q(z) versus the number of ovipositions

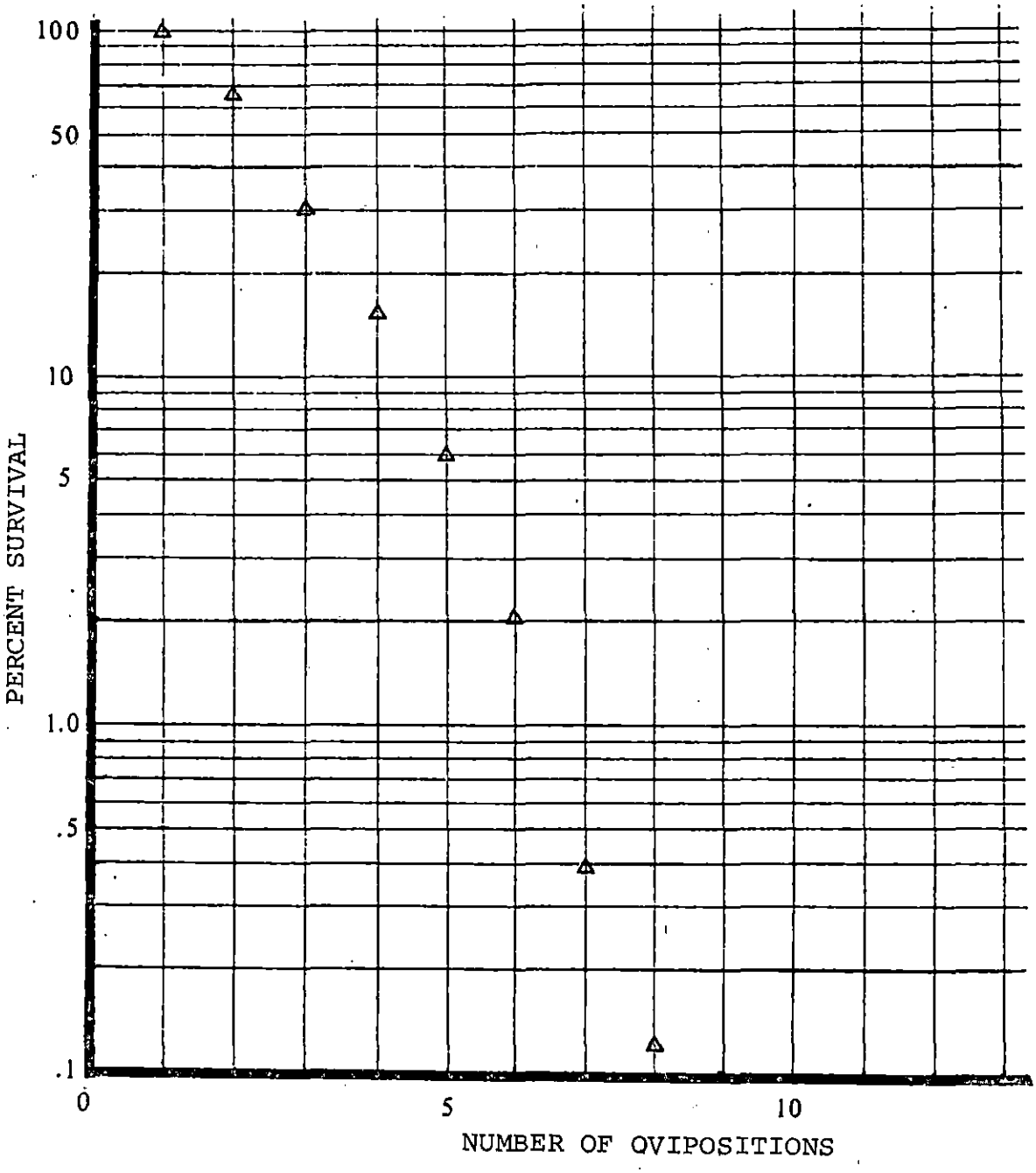


Figure 5. A. gambiae at Gonja; percent survival versus the number of ovipositions

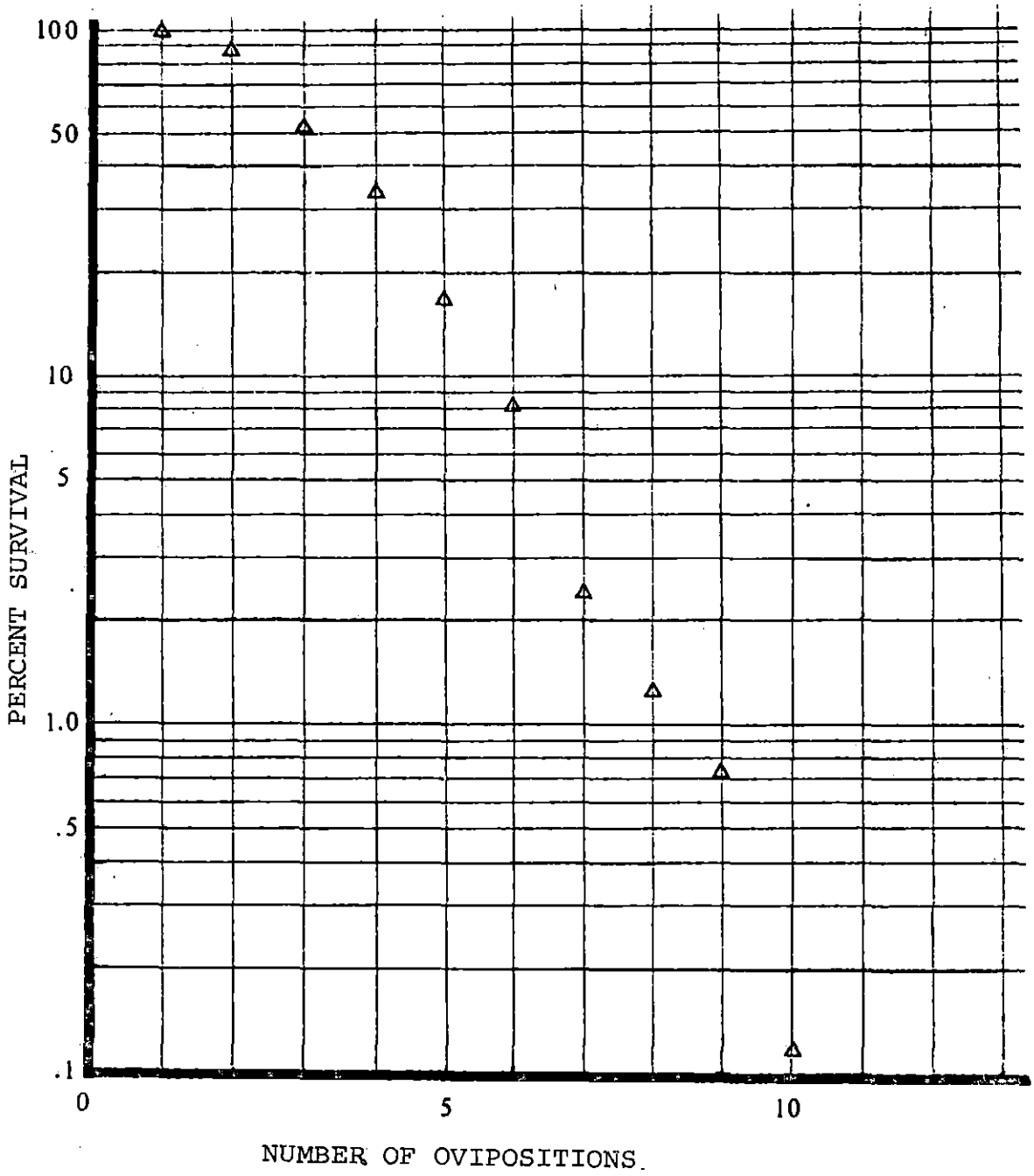


Figure 6. A. funestus at Muheza; percent survival versus the number of ovipositions

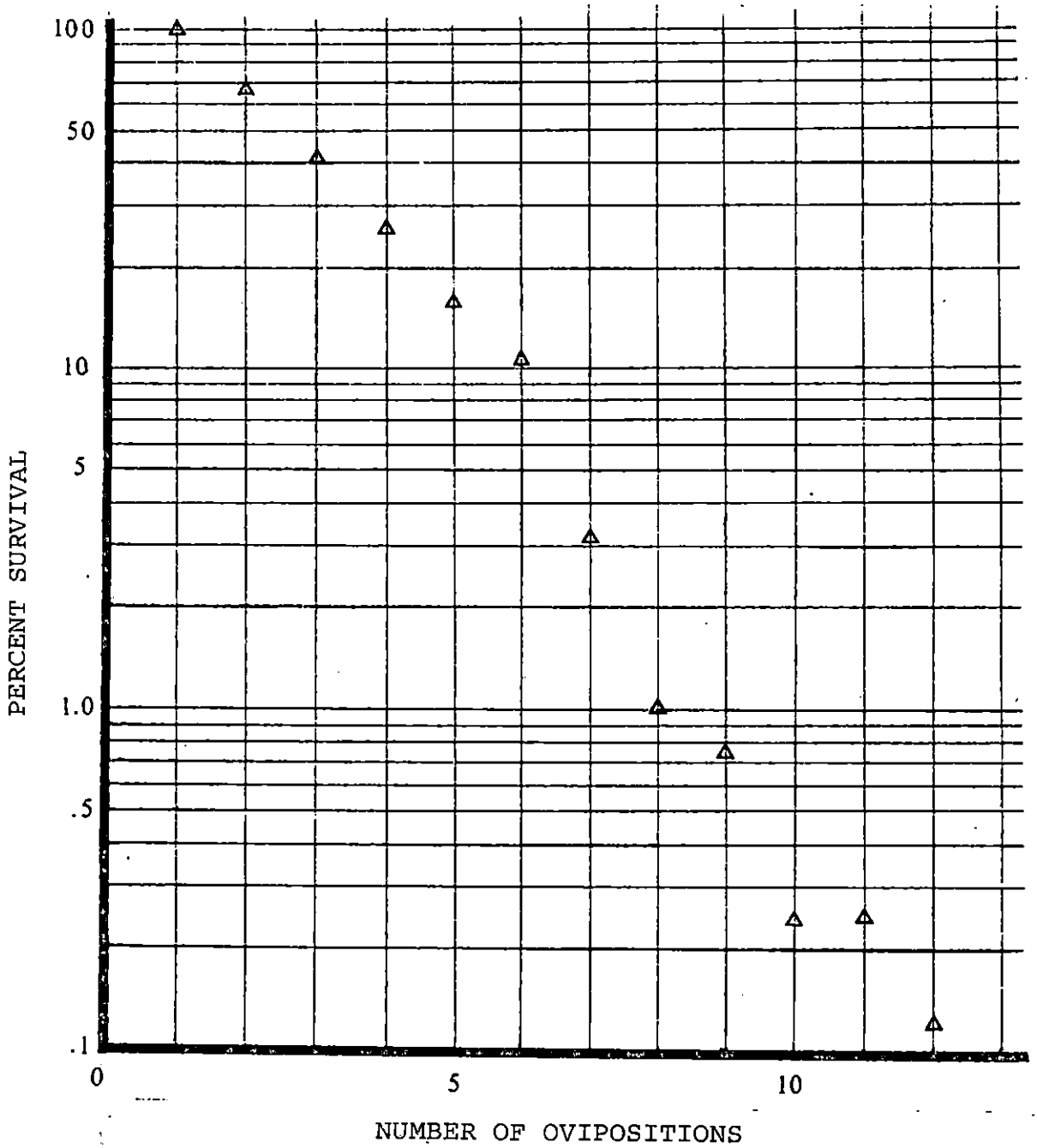


Figure 7. A. gambiae at Muheza; percent survival versus the number of ovipositions

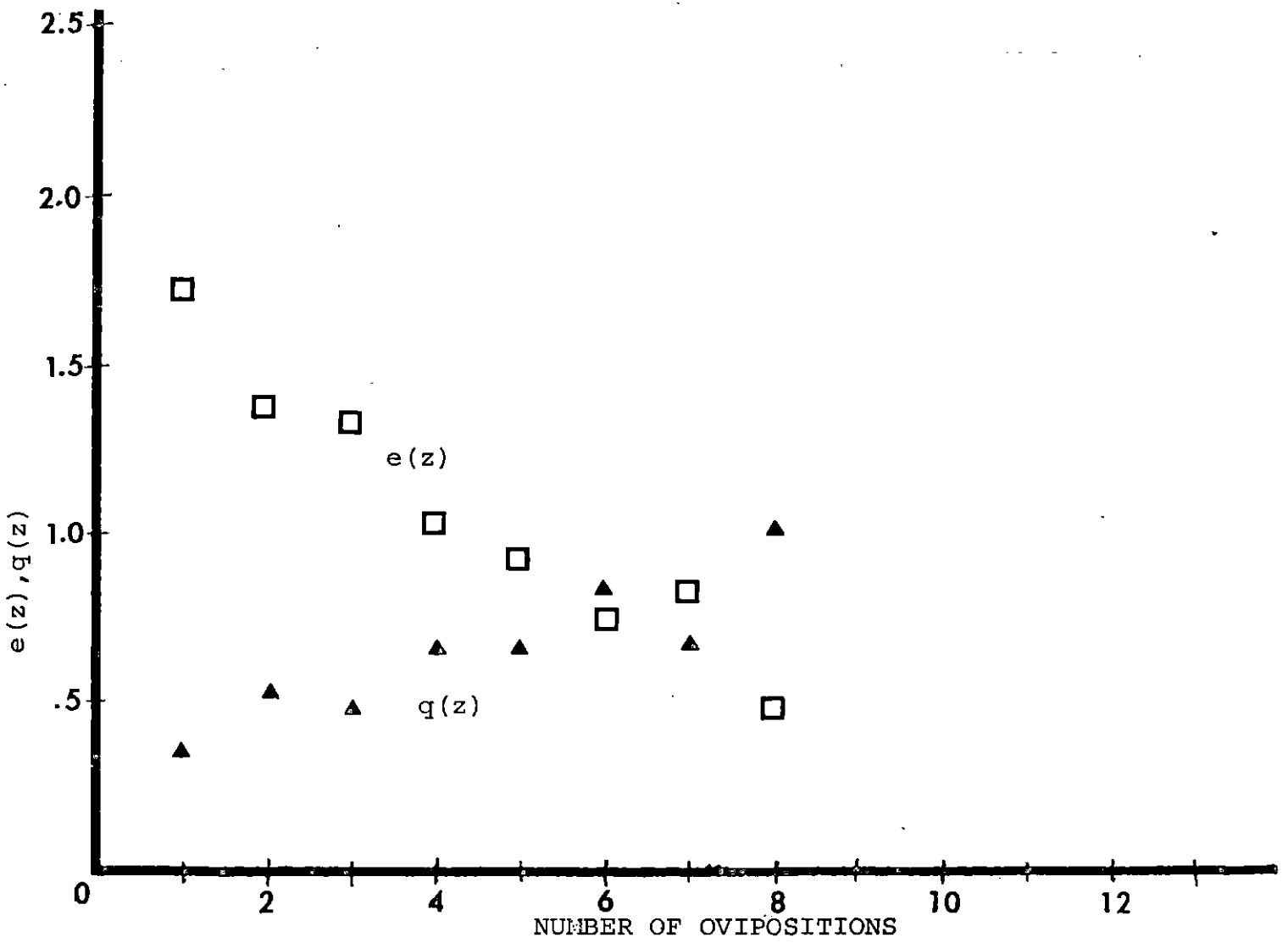


Figure 8. A. gambiae at Gonja; expected life, e(z) and presumptive mortality, q(z) versus the number of ovipositions

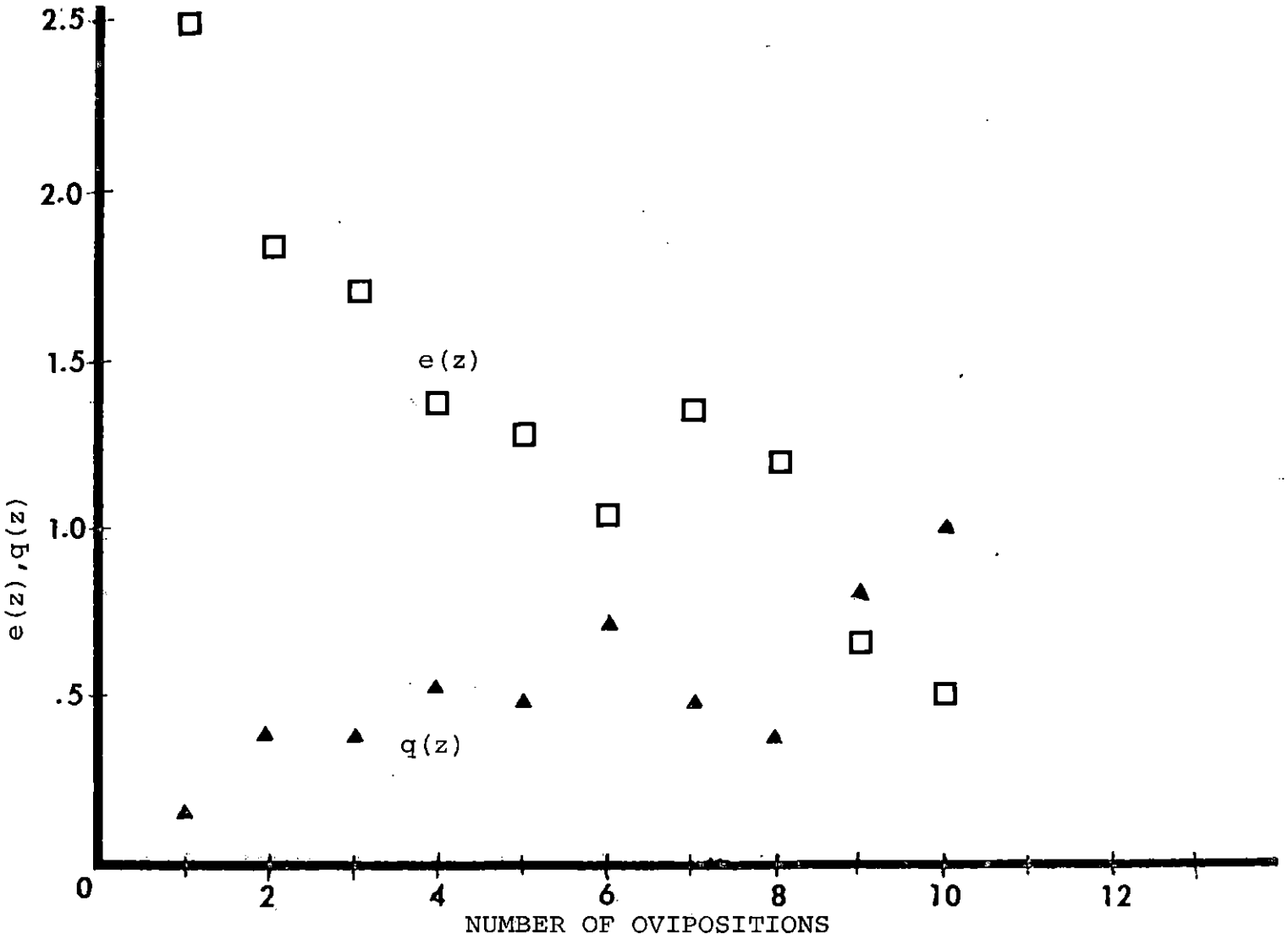


Figure 9. A. funestus at Muheza; expected life e(z) and presumptive mortality q(z) versus the number of ovipositions

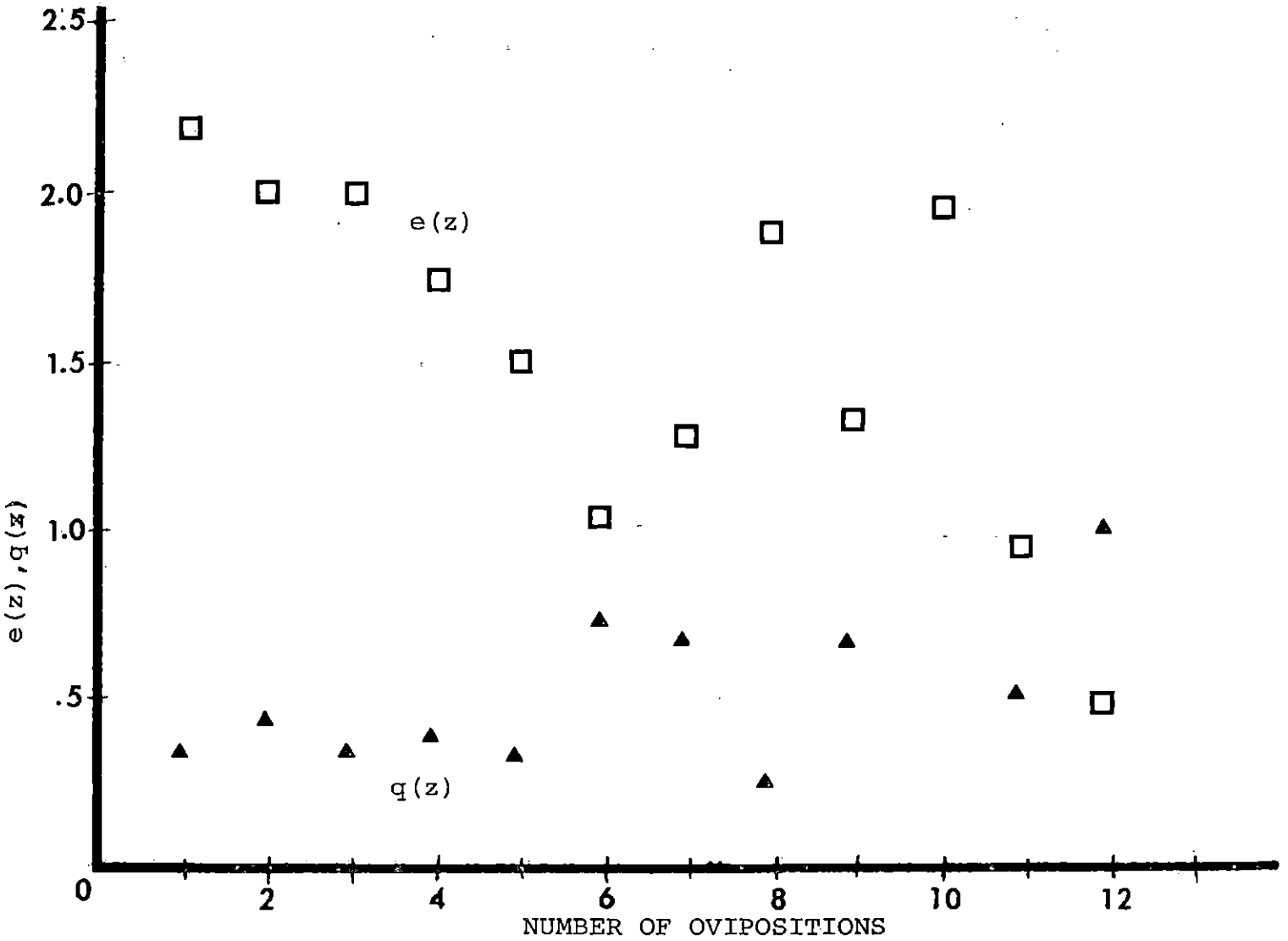


Figure 10. A. gambiae at Muheza; expected life e(z) and presumptive mortality q(z) versus the number of ovipositions

reveals a constant value for all number of ovipositions. The plots for the populations of Gillies and Wilkes of q(x) (Figures 8, 9 and 10) show linear trends. Examination of the plots for %S(z), e(z), and q(z), all show a disagreement between expected and observed curves. Therefore, we will attempt to describe the curves with a different model.

2. New model proposal

A straight line is the easiest curve to manipulate and therefore the most common type used in curve fitting. Macdonald's use of semilog paper to plot %S(t), was to suggest the use of such a straight line. Examination of this straight line fit revealed some discrepancies. We then consider nonlinear regression to develop a better model. General types of common curves to consider are polynomials and exponentials or logarithmics (Steel and Torrie, 1960). To find a better model, let us begin by considering the semi-log plots of %S(t) in Figures 5, 6 and 7. The curves could possibly be fit as a graphed polynomial, using two lines. The first part of the curve, that is, the survival of the younger age groups, defining one line, and a second line defining survival of the older age groups. However, a graphed polynomial requires some rationale for changing curves, and for defining at what point the curves change. To say survival rate between the older and the younger age

groups is so drastically different to require a second curve to describe the older age group, is in direct conflict with Macdonald's assumption of constant mortality. Also, the definition of an old and a young age groups may vary with each location, and each individual's judgment. Since the point where the curves change varies between the populations, and the rationale for changing curves is lacking, another curve may better represent the data.

Consider defining the %S(z) curve on semilog paper by a quadratic. This would require the addition of a squared term to the linear equation. The squared term would cause a more rapid fall in the curve as the number of ovipositions increased. This is observed in Figures 5, 6 and 7. To determine if the addition of a squared term adds significantly to the curves' fit, the models were evaluated statistically. This was done using SAS (Statistical Analysis Systems) on the IBM computer at Iowa State University. The sample results and their interpretation follows.

Type I SS is a sequential sum of squares. The first entry (x_1) accounts for a certain amount of variation in the model. The second entry (x_2/x_1) accounts for the amount of variation, due to x_2 after all variation due to x_1 is removed. This pattern continues for the number of variables given.

Table 10. Sample computer run

Source	Type I SS	F-values	PR>F	Type IV SS	F-values	PR>F
variable x_1	(x_1)			$(x_1/x_2,x_3)$		
variable x_2	(x_2/x_1)			$(x_2/x_1,x_3)$		
variable x_3	$(x_3/x_1,x_2)$			$(x_3/x_1,x_2)$		

The F-values for each Type I SS is given in the next column of the printout. This is followed by the probability of rejection because of the F-value. To be 95% certain that the variable in question does contribute to the model, the value in the PR>F column, should be .0500 or less. If PR>F is .0500 or less, we can declare the variable a significant term in the model. A value of .0100 or less indicates a highly significant term.

Type IV SS lists the variation due to each variable after variation due to the other variables is accounted for. If values in this column are compared, it can be determined which term, or terms would best describe the data. The F-value and PR>F are included to aid in recognizing the significance of each term. The PR>F column can be evaluated as indicated in the Type I SS discussion.

Also included in the computer printout are estimates of the coefficients for the terms. From these estimates we can construct a reasonably accurate equation describing the data. Data for the ordinate are in the form ln %S(z). At z = 1, the y-intercept will be ln (100%) because S(1) was set equal to 100%. The exact location of the intercept at z=0 is dependent on the other coefficients. The computer results for the populations will aid in determining if a quadratic equation will satisfactorily model the data.

III. RESULTS AND DISCUSSION

A. Influences on Sporozoite Rate

The first and second derivatives, with respect to s, are listed in Table 11. Field values for a, x, p, s and n range as follows:

$.1 \leq a \leq .5$

$.005 \leq x \leq .1$

$9 \leq n \leq 20$

$.5 \leq p \leq .90$

$.001 \leq s \leq .10$ (Macdonald, 1973, Davidson and Draper, 1953, Garrett-Jones and Shidrawi, 1969, Gillies and Wilkes, 1965).

Subsitution of these values into the first and second derivatives yields a positive or negative answer.

Table 11. Results for the first and second derivatives with respect to s

First derivative	Second derivative
$\frac{ds}{dx} = \frac{s^2(-\ln p)}{x^2 a p^n}$	$\frac{d^2s}{dx^2} = \frac{s^3 2(\ln p)}{x^3 a p^{2n}}$
$\frac{ds}{da} = \frac{s^2(-\ln p)}{a^2 x p^n}$	$\frac{d^2s}{da^2} = \frac{s^3 2(\ln p)}{a^3 x p^{2n}}$
$\frac{ds}{dn} = s(\ln p)$	$\frac{d^2s}{dn^2} = s(\ln p)^2$
$\frac{ds}{dp} = \frac{s}{p}(n + \frac{s}{axp^n})$	$\frac{d^2s}{dp^2} = \frac{(n-1)(n+1)}{p^2}(s) + \frac{2n-1}{axp^{n+2}}(s^2) + \frac{2s^3}{a^2x^2p^{2(n+1)}}$

The first derivative of s with respect to x has a positive value. Therefore, it can be expected, that as the value for x increases, so will the value of s. In other words, as the number of infective bites to the mosquito, x, increases, the proportion of mosquitoes with sporozoites in their glands will also increase. The second derivative has a negative value; this indicates that the rate of change in the sporozoite rate will decrease with each increasing value for x. That is to say that it will take increasingly larger amounts in the proportion of infective bites to cause each corresponding increase in the sporozoite rate. These phenomena were observed and discussed in the series of papers published by Macdonald (1973).

The first derivative with respect to a, is also found to be positive so s will increase as a increases. From this, it can be predicted that as the number of blood meals on man per day increase, so does the value for the sporozoite rate. This phenomena was reported by Davidson (1955). The second derivative is negative; this indicates a decreasing rate of change $(\frac{ds}{da})$ with an increasing value of a. Therefore, the sporozoite rate will increase at a slower rate for each corresponding increase in the number of blood meals taken per day by the mosquito. This was commented on by Macdonald (1973).

The first derivative, with respect to n, is negative.

This shows that as the length of time for the parasite to complete its cycle (n) increases, the sporozoite rate decreases. This is reasonable, because as n increases, the number of mosquitoes surviving n days decreases. With decreasing numbers of mosquitoes to carry sporozoites, the sporozoite rate will decrease. The positive value for the second derivative indicates that as n increases, the change in the sporozoite rate increases with each equal change in n. This can be verified, because with cooler weather, the value for n increases, along with an increasing drop in s. This was reported by Macdonald (1973).

The first derivative of the sporozoite rate, with respect to p, is more complex than the other first derivatives. Evaluation yields a positive value, so that as the value for the probability of survival, p, increases, so does the value of s. This was suggested by Wanson, Wolfs and Lebied (1947). Considering the positive value of the second derivative, it can be expected that increases in p also result in larger increases in the sporozoite rate. This was observed and reported by Macdonald (1973).

Let us determine which variable causes the largest increase in the sporozoite rate. Begin by separating the first derivatives into two groups: those that cause s to increase with their increase, the positive group and those that cause s to decrease with their increases, the negative group.

It is only necessary to consider the positive group, $\frac{ds}{dx}$, $\frac{ds}{da}$ and $\frac{ds}{dp}$. Next, examine the second derivatives for this group. Locate increasing variables that cause an increasing amount of change in s. There is only one term with this effect, p. Therefore, increases in p should cause the largest increases in s. Substitution of actual numerical values yields the same result.

B. Evaluation of the Proposed Model

The survival curves from Gillies' and Wilkes' mosquito population were modeled as quadratic equations: $\ln \%S(z) = b_1 z^2 + b_2 z + b_3$. These equations were submitted for analysis via SAS. The results of analysis are contained in Tables 12-14. The interpretation follows the table.

Table 12. Computer results for A. gambiae at Gonja

Source	Type I SS	F-value	PR>F	Type IV SS	F-value	PR>F
TIME	39.170	1737.62	.0001	0.079	3.51	0.1197
SQTM	1.215	53.92	.0007	1.215	53.92	0.0007

The Type I SS value for TIME, and SQTM indicate that these are highly significant variables for the proposed model. Type IV SS values reveal that for this population,

SQTM, the squared time term, offers a better fit by itself. The addition of TIME, the linear term does account for some variability, but not a significant amount after variability due to SQTM is removed. A combination of linear and squared terms, i.e., a quadratic, offers a better model than either term by itself. In this case the quadratic form describes the data significantly better than a linear form.

Best Model for Population: $\ln \%S(z) = 4.88 - .20z - .085z^2$

Table 13. Computer results for A. funestus at Muheza

Source	Type I SS	F-value	PR>F	Type IV SS	F-value	PR>F
TIME	44.324	792.14	0.0001	0.106	1.90	0.2105
SQTM	1.431	25.59	0.0015	1.431	25.59	0.0015

Values of Type I SS suggest that TIME and SQTM are both significant. To further determine their significance, observe the Type IV SS. The SQTM variable offers the best model by itself, but TIME helps model the curve more than in the first case. Final choice for description of data is the quadratic form.

Best Model for Population: $\ln \%S(z) = 4.894 - .16z - .05z^2$

Table 14. Computer results for A. gambiae at Muheza

Source	Type I SS	F-value	PR>F	Type IV SS	F-value	PR>F
TIME	61.298	499.97	0.0001	1.935	15.79	0.0032
SQTM	0.168	1.38	0.2710	0.168	1.38	0.2710

In this case, values for Type I SS shows TIME is significant in the fit. Further investigation via Type IV SS reveals that addition of the SQTM term does not add significantly to the fit of the model. For this population, a linear description is adequate.

Best Model for
Population: ln %S(z) = 5.322 - .5z

The second-order term added significantly to the model of the curve in two out of three populations. Let us compare the semilog plots of %S(z) between the proposed model, $S(z) = e^{-(b_1 z^2 + b_2 z)}$ (see Figure 11) and the survival plots from Gillies and Wilkes (Figures 5, 6 and 7). The plots compare favorably. A special case for this model is when the second-order term is not significant, then the model becomes Macdonald's survival curve, $S(z) = e^{-b_2 z}$. The decrease in S(z) due to the second-order term can be a resultant of the environment. A harsher environment may cause the survival rate to decrease more rapidly with age. The rate of decrease for the survival rate is increased by

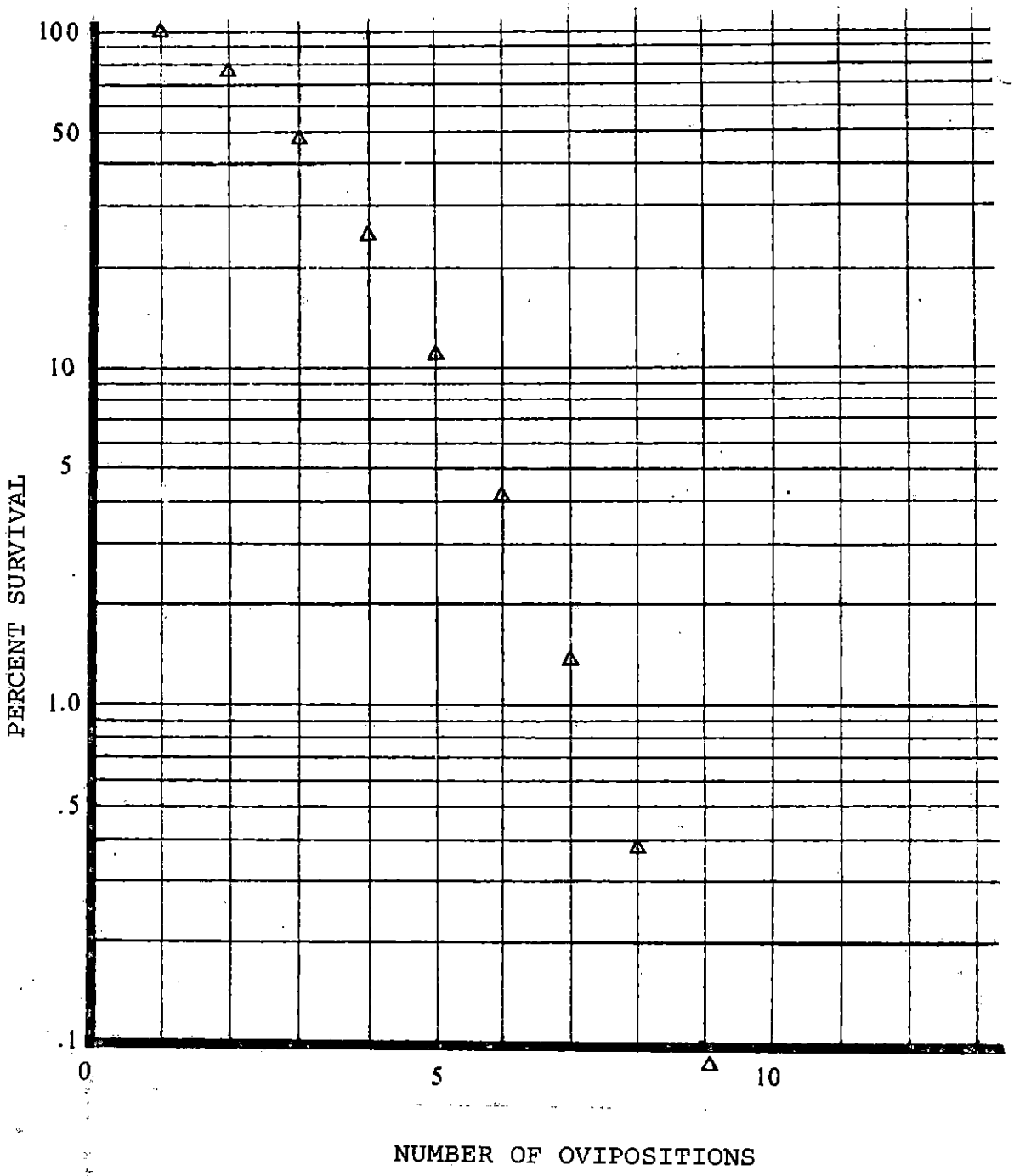


Figure 11. Proposed model, percent survival versus the number of ovipositions

the significance of the second-order term.

To model the curve, each value for z and for S(z) was given equal weight. The S(z)-values for the younger age groups have less error than the S(z)-values for the older age groups in the sample population. This difference in variability is due to the number of samples used to determine each S(z)-value. We must also consider the difficulty in deciphering the age of the older age groups. The size of the samples for the older age groups is such that the addition or loss of a mosquito to a group can noticeably alter their S(z)-values. Look at the figures (Figures 8, 9 and 10) from Gillies' and Wilkes' data for expected life e(z), and presumptive mortality q(z); notice the more erratic pattern in the older individuals. From the e(z) and q(z) figures one can recognize trends.

We will further examine the fit of the proposed model by comparing presumptive mortality q(z), for the proposed model (see Figure 12) with q(z) for the actual populations (Figures 8, 9, 10). When plotted, q(z) for the proposed model yields a linear trend. The plot of q(z) for A. gambiae at Muheza (see Figure 10) yields the line closest to a constant as would be expected by Macdonald's model. The %S(z) semilog plot indicated that the A. gambiae population at Muheza was closest to Macdonald's simple

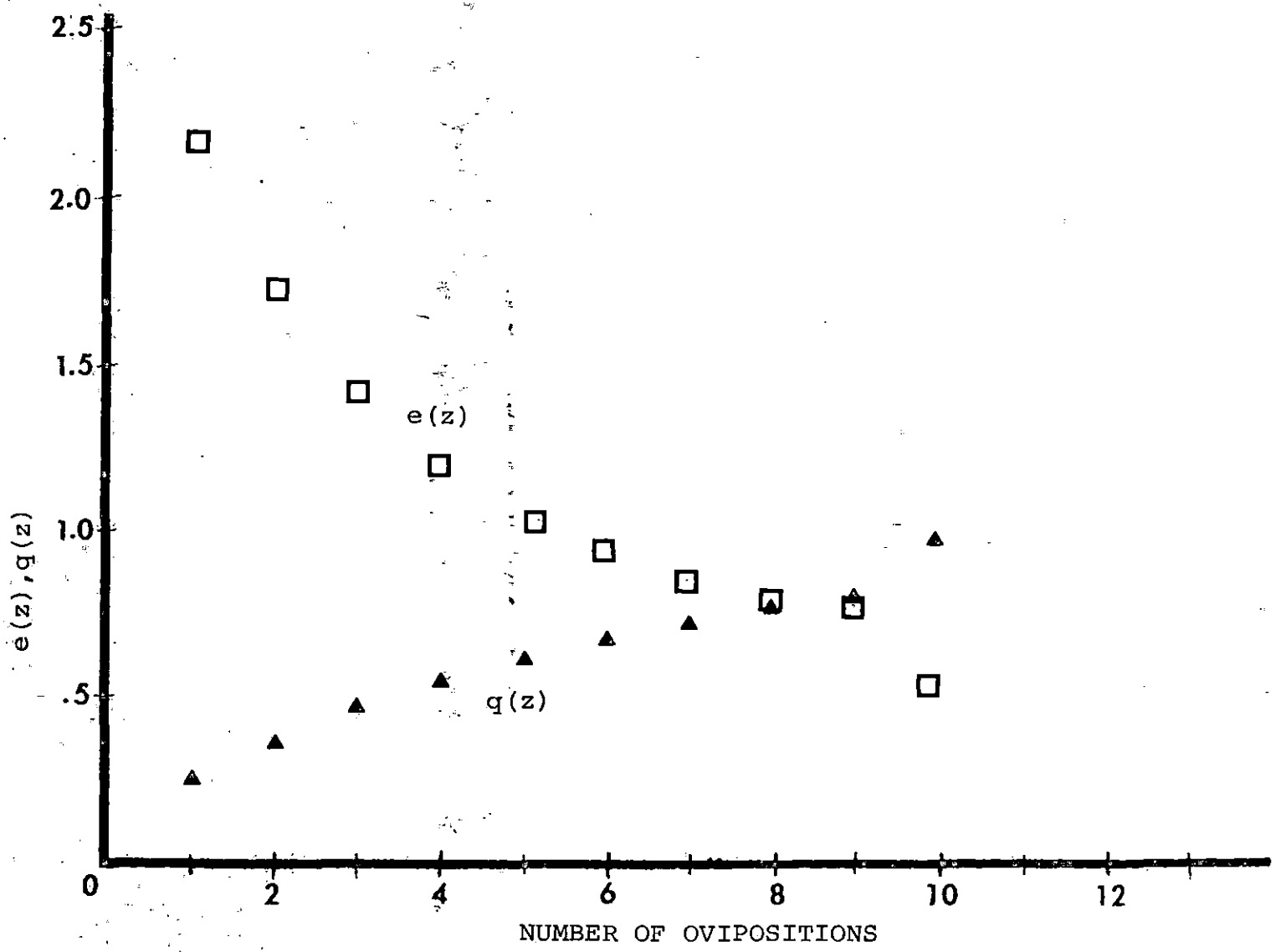


Figure 12. Proposed model, expected life e(z) and presumptive mortality q(z) versus the number of ovipositions

exponential model. The slope of the line in the q(z) plot may be varied by the mortality rate. This rate may vary from population to population or from environment to environment.

In Macdonald's simple exponential model, the expected-life plot remained fairly constant and stable, especially in the younger age groups (see Figure 4). Expected life values for the proposed model (see Figure 12), steadily dropped, beginning with the younger age groups. Examination of the three sample populations (Figures 8, 9, 10), also shows a drop for expected life values, beginning with the younger age groups. Therefore, the e(z) distribution supports the proposed model. All three types of examination indicate that the proposed model is a reasonable hypothesis for the sample populations.

The area under Macdonald's survival curve is larger than the area under the proposed survival curve. As time progresses, the proposed survival curve drops more rapidly than Macdonald's survival curve and the area difference between the two curves increases. Since the proposed model more closely represents most actual biological survival curves; Macdonald's survival curve will overestimate any population that is better modeled by a quadratic equation than a linear one. Use of the linear equation can result in inflated s

values for these populations. The proposed survival curve for mosquitoes should result in more accurate values for s. To further evaluate the proposed survival curve model, more testing with other mosquito populations is necessary.

C. Effect of the New Survival Curve on Sporozoite Rate

Accepting that the survival curve, $S(z) = e^{-(b_1 z^2 + b_2 z)}$ is a more complete description than $S(t) = e^{-vt}$, we can then obtain a more generalized sporozoite equation. We start by defining a new death density function f(z); $f(z) = -S'(z) = -(-2b_1 z - b_2)e^{-(b_1 z^2 + b_2 z)}$. Multiplying f(z) times the probability of infective feeds will give us a new formula for s, the sporozoite rate. We integrate this quantity from n to infinity with respect to time. Then,

$$s = \int_n^\infty (2b_1 z + b_2)e^{-(b_1 z^2 + b_2 z)} (1 - e^{-ax(t-n)})dt$$

where b_1 and b_2 are coefficients describing the survival curve for the population. Also, $t = g_1 z + t_o$; where z = physiological age, i.e. the number of ovipositions, g_1 =

Table 15. Simulated data set for proposed model $S(z) = e^{-(b_1 z^2 + b_2 z)}$

$N(z) = N_o e^{-(b_1 z^2 + b_2 z)}$, $N_o = 1000$, $b_1 = .085$, $b_2 = .200$

z	l(z)	%S(z)	d(z)	L(z)	T(z)	e(z)	q(z)
1	1000.00	100.00	24.80	87.60	216.27	2.163	.248
2	752.01	75.20	27.49	61.46	128.67	1.711	.366
3	477.11	47.71	22.17	36.62	67.21	1.409	.465
4	255.38	25.54	14.01	18.54	30.59	1.198	.549
5	115.32	11.53	7.14	7.96	12.05	1.045	.619
6	43.94	4.39	2.98	2.90	4.09	.932	.679
7	14.12	1.41	1.03	.90	1.19	.844	.730
8	3.83	.38	.30	.23	.29	.765	.770
9	.88	.08	.06	.05	.06	.75	.807
10	.17	.02	.02	.01	.01	.50	1.00
11	.03	.00	-	-	-	-	-

days between z and z+1 parous, t = time in days, and t_0 = initial age of the mosquito at the start of the gonotrophic cycle. In Gillies' and Wilkes' case, t = 3z + 1, the variables a, x, and n remain as defined by Macdonald. After integration, we arrive at

$$s = c_1\sqrt{\pi/d_1}\ (1-\Phi(\sqrt{2d_1}(n+c_2)))$$

where,

$$c_1 = (ax)e(d_1(\frac{d_2+ax}{2d_1})^2 - axn + d_3)$$

$$c_2 = \frac{d_2+ax}{2d_1} \qquad \text{In Gilles and Wilkes case}$$

$$d_1 = \frac{b_1}{(g_1)^2} \qquad d_1 = b_1/9$$

$$d_2 = \frac{2b_1t_0 + g_1b_2}{(g_1)^2} \qquad d_2 = \frac{-2b_1t_0 = 3b_2}{9}$$

$$d_3 = \frac{b_1(t_0)^2-g_1b_2t_0}{(g_1)^2} \qquad d_3 = \frac{b_1t_0^2 - 3b_2t_0}{9}$$

This can be recognized as a function containing a cumulative normal distribution, which is "a convenient tool in modeling random experiments. It can be used to find probabilities of events defined in terms of its corresponding random variables" (Mood, Graybill and Boes, 1963). We can evaluate Φ via the cumulative normal distribution tables.

Many biological phenomena have been analyzed this way.

At Muheza, Gillies and Wilkes measured n = 13, a = .33, s = .0235 and calculated x = .092 for A. funestus and x = .1135 for A. gambiae. These values for a, x, and n are substituted into the new sporozoite model, along with the coefficients b_1 and b_2 for A. funestus. The calculated value of s for A. funestus is .0113. This value for s is not unreasonable. The difference between the measured and calculated s may easily be due to the calculated value of x being incorrect. Next, the values of a, x, n, and the coefficients b_1 and b_2 for the A. gambiae population at Muheza were substituted. The calculated value for s is .13386, which is a high value. The value of b_1 for this population is small compared to b_2, causing the term evaluated by the cumulative distribution to increase.

Also, because of the small value of b_1, with respect to b_2, the value for the c_1 and $\sqrt{\pi/d_1}$ terms become very large. The accuracy of this s value is therefore questionable.

The new sporozoite model allows calculations of a reasonable sporozoite rate, when the survival curve for the population is significantly better modeled by a quadratic equation than by a linear equation. The linear equation for the survival curve gave a questionable result for the sporozoite rate calculated by the new model. The proposed

sporozoite model appears to be reasonable.

Macdonald's model attempted to relate a number of factors affecting the sporozoite rate. The factor n is dependent on the temperature and cannot be controlled. Factors a and x are dependent on the contact between man and mosquito. The factor p was assumed by Macdonald to be constant with respect to time. For the proposed model p is a function of time. The new sporozoite model with p as a function of time appears acceptable, however, it requires more testing to further evaluate its validity.

IV. CONCLUSION

Macdonald's model was examined for validity. Results from mathematical investigations were substantiated with several biological examples. The survival curve for three populations of mosquitoes was evaluated, and it was found as Gillies and Wilkes had surmised, that the survival rate can change with age. A better model for this phenomena was found to be $S(z) = e^{-(b_1 z^2 + b_2 z)}$. Substitution of this survival curve into Macdonald's original s model yielded a new sporozoite model, $s = c_1\sqrt{\pi/d_1}\ (1-\Phi(\sqrt{2d_1}(n+c_2)))$. This model was examined with data available from Gillies' and Wilkes' 1965 paper. Results from the model reveal that this is an acceptable model if the survival curve is of the form $S(z) = e^{-(b_1 z^2 + b_2 z)}$. It is a questionable model if b_1 is not significant with respect to b_2, so that $S(z) = e^{-(b_2 z)}$ is used to represent the survival curve. Further evaluation in the field is necessary to prove its usefulness.

V. REFERENCES

Alvarado, C. and L. J. Bruce-Chwatt. 1962. Malaria. Scientific American 206, No. 5: 86-98.

Armitage, P. 1953. A note on the epidemiology of Malaria. Trop. Dis. Bull. 50, No. 10:890-892.

Bailey, N. T. J. 1975. The mathematical theory of infectious diseases and its applications. 2nd ed. Griffin, London.

Boyd, M. F. 1949. Epidemiology: factors related to the definitive host. Pg. 608-697 in M. F. Boyd, editor. Malariology. W. B. Saunders, Philadelphia.

Coatney, G. R., W. E. Collins, M. W. Warren and P. C. Contacos. 1971. The primate malarias. Government Printing Office, Washington, D.C.

Daly, H., J. Doyen and P. Ehrlich. 1978. Introduction to Insect Biology and Diversity. McGraw-Hill, New York.

Davidson, G. 1955. Further studies of the basic factors concerned in the transmission of malaria. Trans. R. Soc. Trop. Med. Hyg. 49: 339-350.

Davidson, G. and C. C. Draper. 1953. Field studies of some of the basic factors concerned in the transmission of malaria. Trans. R. Soc. Trop. Med. Hyg. 47, No. 6: 522-535.

Detinova, T. S. 1962. Age-grouping methods in Diptera of medical importance with special reference to some vectors of malaria. Monogr. Ser. World Hlth. Org. No. 47.

Garnham, P. C. C. 1966. Malaria parasites and other haemosporidia. Blackwell Scientific, Oxford.

Garrett-Jones. C. 1964. The human blood index of malaria vectors in relation to epidemiological assessment. Bull. Wld. Hlth. Org. 30: 241-261.

Garrett-Jones, C. and G. R. Shidrawi. 1969. Malaria Vectorial Capacity of a Population of Anopheles gambiae. Bull. Wld. Hlth. Org. 40: 531-545.

Gillies, M. T. and T. J. Wilkes. 1965. A Study of the Age-composition of Populations of Anopheles gambiae and A. funestus giles in North-Eastern Tanzania. Bull. Ent. Res. 56: 237-263.

Gross, A. and V. Clark. 1975. Survival distributions reliability applications in the biomedical sciences. John Wiley and Sons, New York.

Gruchet, H. 1962. Étude de l'age physiologique des femelles d'Anopheles funestus Giles dans la région de Miandrivazo, Madagascar. Bull. Soc. Path. Exot. 55: 165-174.

Hamon, J., G. Chauvet, and L. Thélin. 1961. Observations sur les méthodes d'évaluation de l'âge physiologique des femelles d'anophelès. Bull. World Hlth. Org. 24: 437-443.

Harrison, Gordon A. 1978. Mosquitoes, malaria, and man. Dutton, New York.

Jones, A. 1967. Introduction to Parasitology. Addison-Wesley, London.

Knight, K. and A. Stone. 1977. A catalog of the mosquitoes of the world (Diptera: Culicidae). 2nd Ed. Entomological Society of America, College Park, Md.

Larson, J. 1974. Introduction to Probability Theory and Statistical Inference. 2nd ed. John Wiley & Sons, New York.

Macdonald, G. 1950. The analysis of malaria parasite rates in infants, Trop. Dis. Bull. 47:907-915.

Macdonald, G. 1952. The analysis of the sporozoite rate. Trop. Dis. Bull. 49:569-586.

Macdonald, G. 1973. Dynamics of tropical disease. Edited by L. J. Bruce-Chwatt and V. J. Glanville. Oxford University Press, London.

Mood, A., F. Graybill and D. Boes. 1963. Introduction to the theory of statistics. 3rd ed. McGraw-Hill Book Co., New York.

Muench, H. 1959. Catalytic Models in epidemiology. Harvard University Press, Cambridge.

Ott, L. 1977. An introduction to Statistical Methods and Data Analysis. Duxbury Press, North Scituate, Mass.

Southwood, T. R. E. 1978. Ecological methods. 2nd ed. Wiley, New York.

Steel, R. and J. Torrie. 1960. Principles and Procedures of Statistics. McGraw-Hill Book Co., New York.

Swaroop, S. 1966. Statistical methods in malaria eradication. World Health Organization, Geneva.

Wanson, M., J. Wolfs and B. Lebied. 1947. Comportement de l'Anopheles (Myzomyia) Moucheti Evans. Rec. Sci. Mid. Congo Belge. 6:39.

White, G. B. 1979. Identification of mosquitoes as vectors of malaria and filariasis. Pg. 103-143 in A. E. R. Taylor and R. Muller, eds. Problems in the identification of parasites and their vectors. Blackwell Scientific, Oxford.