Theor Appl Genet (1991) 82:368–378

Simulation of genetic control. Homozygous-viable pericentric inversions in field-female killing systems

G. G. Foster

CSIRO, Division of Entomology, GPO Box 1700, Canberra 2601, Australia

Received November 23, 1990; Accepted February 20, 1991
Communicated by J. S. F. Barker

Summary. The GENCON simulation program GC5 is designed to simulate genetic population control using field-female killing (FK) systems carying pericentric inversions in addition to Y-linked translocations and deleterious mutations. Homozygous-viable pericentric inversions are included on the same chromosomes as the deleterious mutations, in repulsion to the Y-linked translocation. Released males transmit the inversions and mutations to their daughters and the translocation to their sons. Daughters are semisterile regardless of the type of male they mate with, because products of crossing-over within the inversions carry inviable duplications and deficiencies. Compared to present FK systems, inversion-containing strains give higher levels of genetic death, with both faster initial suppression and greater persistence of genetic death from field-reared descendants if releases are interrupted. At low release rates, both types of FK system are more effective than sterile males.

Key words: Genetic control – Simulation – Translocation – Inversion – Genetic sexing

Introduction

Genetic sexing systems enable killing or sorting of mass-reared insects according to sex, usually by linking sex with mutations using rearrangements between the Y and other chromosomes. They have potential application both in rearing economically important insects such as silkworms (Tazima 1964), and in genetic pest control strategies involving release of sterilized or genetically altered males (reviewed by Whitten and Foster 1975).

In Australia, a genetic sexing system that operates in the field currently forms the basis for proposed large-scale control programs against the sheep blowfly *Lucilia cuprina*, a major pest of the Australian sheep industry (Whitten et al. 1977; Whitten 1979; Foster et al. 1985, 1988; Foster 1989). These field-female killing (FK) systems combine recessive eye-color mutations with a Y-linked translocation. Females are homozygous for the mutations and have white eyes. They are functionally blind, and while they can survive in cages, they rarely survive long in the field (Whitten et al. 1977).

Males carry the wild-type alleles of the eye mutations on the translocation, and carry the mutations on a normal set of autosomes. They have normally pigmented eyes and are competitive in the field, transmitting the translocation to their sons and the mutations to their daughters. When a daughter, heterozygous for the mutations, is mated by a released male, half or more (depending on the number of mutations used) of her daughters are homozygous and thus unable to survive to reproductive maturity (see Fig. 1 of Foster et al. 1988).

Release of FK-strain males into field populations leads to reduced population fertility from the semisterility of the translocations and, eventually (with sustained releases), homozygosis for the mutations in a high proportion of nontranslocation zygotes of field origin (Whitten et al. 1977; Whitten 1979; Foster et al. 1985, 1988). Semisterility and homozygosis combine to give genetic death rates approaching 94% with presently available strains. This type of system has been successfully used to suppress sheep blowfly populations in two field trials conducted in 1984–1986 (R. J. Mahon, T. L. Woodburn, and G. G. Foster, unpublished results).

For long-term suppression campaigns, FK systems are likely to be more cost-effective than the sterile-insect technique (SIT), since at low release rates they give rise to higher genetic death rates in density-influenced populations (Foster et al. 1988). This may make control of the screwworm fly *Cochliomyia hominivorax* more economi-

cally feasible in South America and in North Africa, if present eradication attempts in Libya using SIT should fail to prevent spread of the current infestation (Foster 1991). Moreover, since released females die before reproductive maturity, the use of FK systems would reduce or eliminate many problems encountered with present SIT programs, including the need for rearing-plant security against releasing fertile insects, and biting (mosquitoes) or ovipositor puncture of fruit (fruit flies) by released sterilized females.

Genetic sexing systems for higher Diptera have generally relied on low levels of male crossing-over to maintain the phenotypic differentiation between the sexes (Whitten 1969, 1979; Whitten et al. 1977; Robinson and Van Heemert 1982). However, it is now recognized that such systems are too unstable for practical mass-rearing in large-scale control programs. Recombination in males, followed by selection of fitter genotypes, leads to breakdown of the strains in rearing colonies (Foster et al. 1980, 1991; Rossler 1982a, b; Hooper et al. 1987; Busch-Petersen 1989). Inclusion of inversions to eliminate the products of recombination, a routine practice in mosquitoes, may provide a solution to this problem (Curtis 1968; Robinson 1975; Curtis et al. 1976; Baker et al. 1979, 1980; Kaiser et al. 1978; Foster 1991).

Of several options available for including inversions in FK systems, homozygous-viable pericentric inversions appear to be the best choice (Foster 1991). The current plan involves constructing strains (Fig. 1a) in which a Y-autosome translocation carring the wild-type alleles of the critical mutations (w^+ and yw^+ shown here) is balanced against a homozygous-viable inversion containing the mutant alleles of both loci. This is similar in karyotype to strains constructed in two *Anopheles* species by Baker et al. (1980) and Suguna et al. (1981). A large, homozygous-viable pericentric inversion will be included on one or more of the nontranslocated chromosomes carrying the eye color mutations. Females will be homozygous for the inversion and mutations, while males will be heterozygous for both, in repulsion to the Y-linked translocation.

In addition to suppressing male recombination, the pericentric inversion(s) should significantly increase the rate of genetic death imposed on field populations. Field-reared daughters of released males would be heterozygous for the inversions. They would be semisterile regardless of what type of male they mated with, because crossing-over within the inversions would generate inviable duplication/deficiency gametes (Robinson 1975; and see Fig. 1b). The expected semisterility is half the frequency of tetrads containing at least one exchange event within the inverted segment, giving a maximum 50% heterozygote sterility.

This paper describes simulations, using a modified GENCON program (Foster et al. 1988) designed to explore the suppressive potential of FK strains containing pericentric inversions.

Materials and methods

The simulation program GC5

General description. GC5 performs similar calculations to those done by GC1 (Foster et al. 1988). Starting with a finite test population and using discrete generations, GC5 computes the effects on population size and genotype frequencies of matings between wild females and released males and their descendants, under the influence of various ecological and genetic variables. Permitted ecological variables include migration, weather effects, and density dependence. Genetic variables include translocation and inversion semisterility or the level of irradiation-induced sterility, and the number and linkage relationships of mutations and rearrangements.

The major differences between GC1 and GC5 involve changes to the main program and the genetic subroutines PROVA5, PSPERM5, ZYGOTE5, and GENEXT5, necessary to simulate crossing-over within heterozygotes for pericentric inversions on chromosome 3 of *L. cuprina* (Fig. 1b).

Assuming random mating, the program pairs each possible female and male genotype. For each mating type, four genetic subroutines are called: PSPERM5 and PROVA5 assign gamete probabilities to each chosen male and female genotype, respectively; ZYGOTE5 assigns zygote probabilities based on the assigned gamete probabilities; then GENEXT5 computes the numerical contribution of each mating type to the next generation.

Exchange within inversions. The frequencies of various exchange types within inversion heterozygotes are derived from input parameters *a*, *b*, and *c*, which are the respective probabilities of at least one exchange occurring within the genetically defined regions I, II, and III (Fig. 1c), plus an expression to simulate coincidence (Co) of simultaneous exchanges in regions I and II (Stevens 1936). Exchange in region III is considered independent of exchange in the other two regions (coincidence = 1.0), since they are separated by the centromere (Stevens 1936; Foster et al. 1981).

The frequencies of each exchange type (E_i) are calculated as detailed below.

$$E_A = a \cdot (1-b+R_A) \cdot (1-c)$$
$$E_B = b \cdot (1-a+R_B) \cdot (1-c)$$
$$E_C = c \cdot (1-a) \cdot (1-b)$$
$$E_{AB} = a \cdot b \cdot (1-c) \cdot \mathrm{Co}$$
$$E_{AC} = a \cdot c \cdot (1-b+R_A)$$
$$E_{BC} = b \cdot c \cdot (1-a+R_B)$$
$$E_{ABC} = a \cdot b \cdot c \cdot \mathrm{Co}.$$

Coincidence is approximated from an empirical formula derived using data from *L. cuprina* (Foster et al. 1981 and unpublished results), as outlined below:

$$X = (a+b)/2$$

if $X \leqq 0.35$, $\mathrm{Co} = 0.$

if $X \geqq 0.70$, $\mathrm{Co} = 1.0$

otherwise, $\mathrm{Co} = (X-0.35)/0.35.$

The terms R_A and R_B allow for the reduction caused by interference (1 − Co) between simultaneous exchanges in regions I and II. Given that an exchange in region I has occurred, the

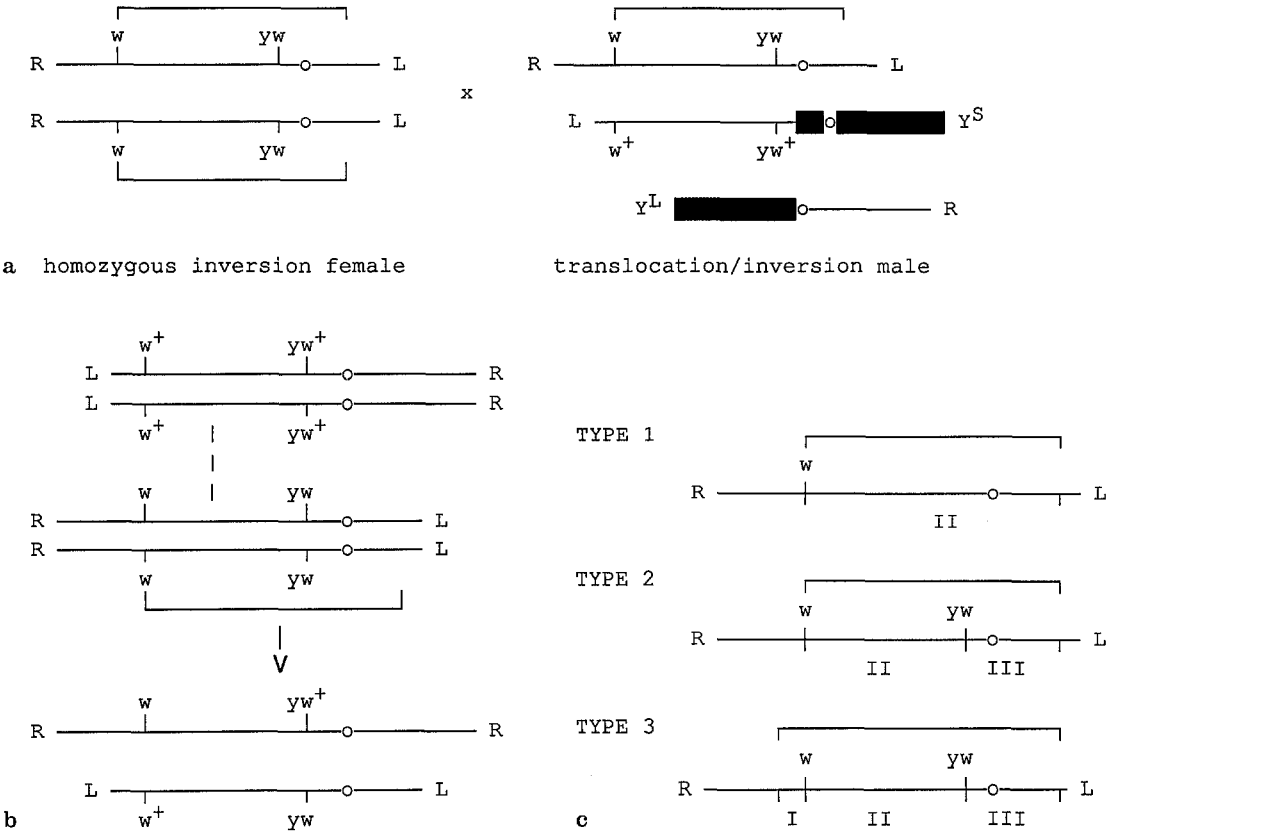

Fig. 1 a–c. Diagrams of karyotypes mentioned in the present paper. Centromeres indicated by *circles*; L, R – *left* and *right* arms of chromosome 3 of *L. cuprina*; square brackets indicate inverted sequence; Y chromosome shaded; Y^L, Y^S – long and short arms of the Y, respectively; w, yw – white, yellowish eye mutations, respectively (superscript + = wild-type alleles). **a** Karyotypes of males and females in inversion-containing FK strain. **b** Generation of duplication/deficiency chromosomes by crossing-over within pericentric inversion. **c** Types of pericentric inversions used in simulations: type 1 – inversion with one mutation only, sited at inversion break point, meiotic exchange in region II; type 2 – inversion containing two mutations, one of which is sited at inversion break point, meiotic exchange in regions II and III; type 3 – inversion containing two mutations, with meiotic exchange in genetic regions I, II, and III

probability of *no exchange in region II* is increased by the value R_A. Similarly, R_B is the reduction of the probability of an exchange occuring in region I, given that one has occurred in region II. These values are calculated as follows.

$$R = (a \cdot b) - (a \cdot b \cdot \mathrm{Co})$$

$$R_A = a \cdot R/(a+b)$$

$$R_B = b \cdot R/(a+b).$$

The frequencies of viable crossover products from exchange within inversion heterozygotes are calculated in the female gametic subroutine PROVA5, using double-crossover factors (D_i) calculated in the main program as follows.

For w yw/+ + and w+/+ yw heterozygotes:

$$D_{AB1} = 0.5\,(E_{AB}) + 0.25\,(E_{ABC})$$

$$D_{AC1} = 0.5\,(E_{AC}) + 0.25\,(E_{ABC})$$

$$D_{BC1} = 0.5\,(E_{BC}) + 0.25\,(E_{ABC})$$

$$D_{AC2} = D_{AB1} + D_{AC1} + D_{BC1};$$

for w +/+ + heterozygotes:

$$D_{AB2} = 0.5\,(E_{AB} + E_{AC} + E_{ABC});$$

for + yw/+ + heterozygotes:

$$D_{BC2} = 0.5\,(E_{BC} + E_{AC} + E_{ABC}).$$

Genetic death. The genetic death calculations performed in GC5 are similar to those described in Foster et al. (1988) and Foster and Smith (1991). Genetic death from crossing-over in inversion heterozygotes (CD) is calculated from inversion semisterility (S_i) and the proportion of inversion heterozygote females in the locally mated population (P_{if}).

$$\mathrm{ET} = E_A + E_B + E_C + E_{AB} + E_{AC} + E_{BC} + E_{ABC}$$

$$S_i = \mathrm{ET}/2$$

$$\mathrm{CD} = S_i \cdot P_{if}.$$

Translocation genetic death (TD) is calculated from the fertility of the translocation (F_t), the proportion of females among euploid offspring of the translocation (P_f), and the proportion of matings by translocation males (P_{tm}).

$$\mathrm{TD} = (1.0 - F_t \cdot P_f/0.5) \cdot P_{tm}.$$

Genetic death due to homozygosis of mutations (MD) is calculated from the number of mutant (N_m) and viable (N_v) zygotes

generated by the program.

$N_T = N_v + N_m$

$MD = N_m / N_T$.

The frequency of aneuploid zygotes (AN) and genetic death in the locally mated population (GD) are calculated as shown below.

$AN = CD + (1.0 - CD) \cdot TD$

$GD = AN + (1.0 - AN) \cdot MD$.

The program allows for the effects of immigration on genetic death (not used in the present report). Population genetic death (PGD) (after immigration of mated females) is calculated as shown below, where N_{mf} = number of locally mated females and $N_{bf} = N_{mf}$ + mated immigrant females.

$PGD = GD \cdot N_{mf} / N_{bf}$.

Rates of population increase – density effects. GC5 allows three options for determining rate of population increase (RATINC):

(1) density independent (RATINC values each generation specified as input data) (not used in the present paper);

or one of two other options based on Prout's (1978) formula for density dependence:

(2) density dependent (RATINC solely determined by density), according to the formula (Foster et al. 1988):

$$RATINC = R_{MAX} \cdot K / (K + (R_{MAX} - 1) \cdot N),$$

where R_{MAX} is the maximum possible rate of increase, N is the adult female population density, and K is the equilibrium population density; or

(3) density influenced (seasonal rates of increase based on field data, but below a specified population density, RATINC values are multiplied by a density factor, DF); DF is calculated each generation according to the formula (Foster and Smith 1991):

$$DF = DF_{MAX} \cdot K_d / (K_d + (DF_{MAX} - 1) \cdot N),$$

where DF_{MAX} is the maximum density factor and K_d is the population size below which DF is greater than 1.0.

Simulations

In all simulations, initial population size was 10^6 wild individuals of each sex. All simulations were conducted for 40 generations with zero migration. Unless specified otherwise, release rates were uniform (the same number of males released each generation). In all simulations, both the sex ratio and translocation sterility were set at 0.5.

The characteristics of the strains used in simulations are described in 'Results' and summarized in Table 1. In females homozygous for the standard chromosome or the inversion, the crossover frequency between the linked mutations w and yw is assumed to be 0.4744 (Foster et al. 1988).

In simulations with density-dependent populations, R_{MAX} was set at 10. Release rates were 0.5 million or lower per generation, i.e., equal to or less than those in previous simulations (Fig. 5d of Foster et al. 1988) in which sterile males were ineffective.

The simulations with density-influenced population regulation are intended to provide a realistic approximation to controlling *L. cuprina* populations in Australia. It is assumed that density effects in this ecosystem are related to the related to the response of farmers to infestation, rather than limitation of resources available to the immature stages (Foster et al. 1975).

Table 1. Summary of strain characteristics used in simulations

Simulation	Strain type[a]	Number of mutations	Inversion exchange frequency		
			Region I	Region II	Region III
A	SIT	–	–	–	–
B	FK/S	1	–	–	–
C	FK/I	1	0	0.333	0
D	FK/I	1	0	0.667	0
E	FK/I	1	0	1.0	0
F	FK/S	3	–	–	–
G	FK/I	2	0	1.0	0
H	FK/I	2	0	1.0	0.333
I	FK/I	2	0	1.0	0.667
J	FK/I	2	0	1.0	1.0
K	FK/I	3	0	1.0	0
L	FK/I	3	0	1.0	0.333
M	FK/I	3	0	1.0	0.667
N	FK/I	3	0	1.0	1.0
O	FK/I	2	0.333	1.0	0.333
P	FK/I	2	0.333	1.0	0.667
Q	FK/I	2	0.333	1.0	1.0
R	FK/I	2	0.667	1.0	0.667
S	FK/I	3	0.333	1.0	0.333
T	FK/I	3	0.333	1.0	0.667
U	FK/I	3	0.333	1.0	1.0
V	FK/I	3	0.667	1.0	0.667

[a] SIT = sterile insect technique; FK/S, FK/I = field-female killing strains with standard or inversion chromosomes, respectively

The seasonal rates of increase used in the density-influenced populations (6.16, 3.19, 0.40, 0.30, 0.50, 4.00, 4.00, 0.053) are repeated five times. This pattern assumes eight generations per year (Foster and Smith 1991) and represents an annual rate of increase of 1.00. This is based on the bimodal pattern commonly seen in the Canberra region, i.e., conditions favoring increase during spring and autumn, with summer and overwintering population declines (Vogt et al. 1985b). It is assumed that these rates of increase include both weather and density effects within the population-size range usually encountered in this region, i.e., at population above 10^6 females, in terms of the present simulations.

In the simulations, below a population size of 10^6 females (K_d), the above rates of increase were multiplied by DF, calculated using $DF_{MAX} = 5.0$. Multiplying the springtime rate of increase (6.16) by DF_{MAX} gives a maximum rate of increase at low densities of 30.8. This parameter can be estimated independently using data from various ecological studies of *L. cuprina*. Assuming 232 ovarioles and a 12% springtime (October) resorption rate (Vogt et al. 1985a), 85.5% egg hatch (Vogt and Woodburn 1980), 70% survival of larvae on sheep (Dallwitz et al. 1984), 48% survival in the soil (Foster et al. 1975), and that females oviposit once in the field (Kitching 1977), egg-to-egg survival under ideal conditions in populations of *L. cuprina* can be estimated at 29.3. Thus, the simulations using density-influenced population regulation offer a reasonable approximation of genetic control of *L. cuprina* populations.

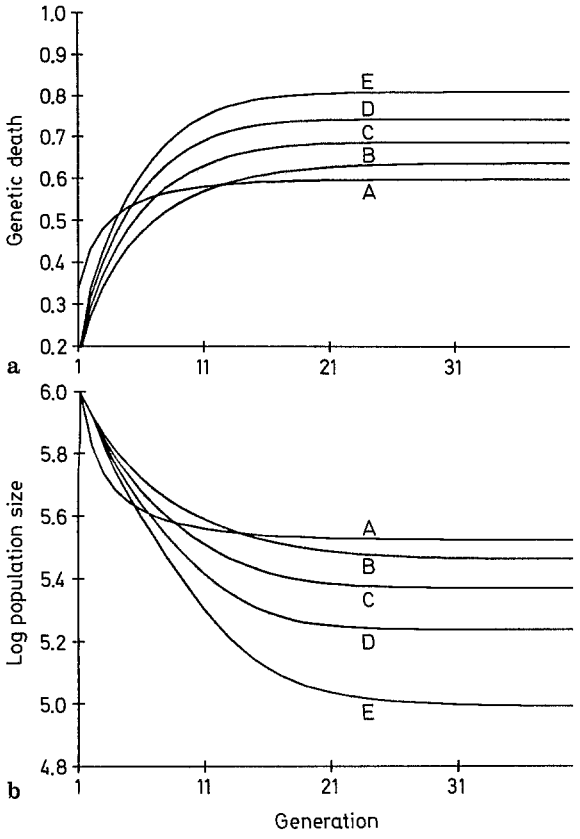

Fig. 2 a and b. Simulations comparing SIT and FK strains containing one mutation tightly linked to the inversion (Type 1, Fig. 1 c). Density-dependent populations; continuous releases 0.5 million per generation for 40 generations; A = sterile males; B = translocation with no inversion and one mutation; C, D, E = translocation with inversion and one mutation, exchange in region II = 0.333, 0.667, 1.0, respectively (see Table 1); **a** genetic death, **b** population size

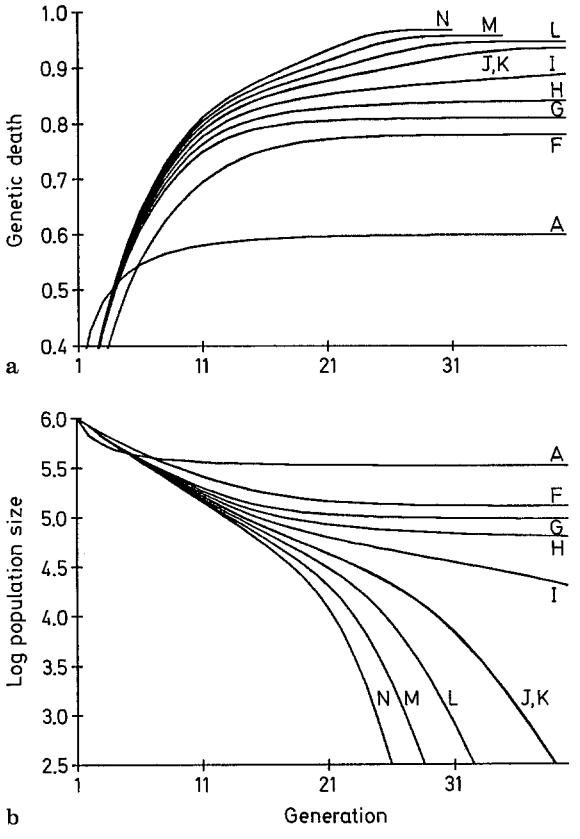

Fig. 3 a and b. Simulations comparing SIT and FK strains containing two mutations within the inversion, with at least one tightly linked to an inversion break point (Type 2, Fig. 1 c). Density-dependent populations; continuous releases 0.5 million per generation for 40 generations; A = sterile males; F = translocation with no inversion and three mutations; G, H, I, J = translocation with inversion containing two mutations, exchange in region III = 0.0, 0.333, 0.667, 1.0, respectively; K, L, M, N = translocation with inversion containing two mutations plus one unlinked mutation, exchange in region III = 0.0, 0.333, 0.667, 1.0, respectively; exchange in region II = 1.0 for all inversions (see Table 1); **a** genetic death, **b** population size

Results

Density-dependent population regulation

Effect of inversion sterility. Simulations of releases of sterile males (SIT) and simple FK systems (translocation with a single mutation), either with an inversion (FK/I) or without an inversion (FK/S), are summarized in Fig. 2. All inversions had one break point at the mutant locus (Type 1, Fig. 1 c).

SIT releases (simulation A Fig. 2) initially gave more rapid suppression than the FK strains, but the latter ultimately gave greater genetic death rates and suppression. The FK/I strains (simulations C–E) produced both more rapid initial suppression and lower final population sizes than the FK/S strain (simulation B). Increasing the inversion size gives progressively greater genetic death and population suppression, until the maximum female sterility of 50% is reached (simulations C–E).

None of the strains simulated in Fig. 2 caused sufficient genetic death to suppress populations to the unstable equilibrium level (Prout 1978), below which eradication is inevitable if releases continue. The final (stable) equilibrium population size with the largest inversion (simulation E, Fig. 2) is an order of magnitude below that with no releases.

Effect of additional mutations. Simulation of strains carrying additional mutations, both within the inversion (Type 2, Fig. 1 c) and on a heterologous chromosome, are summarized in Fig. 3. Simulations of SIT and a three-mutation FK/S strain are included for reference (simulations A and F, respectively). In these and all subsequent simulations of FK/I strains, the frequency of exchange in region II is 100% (giving 50% sterility in inversion heterozygote females in all simulations).

Including a second mutation within the inversion (Type 2, Fig. 1 c) leads to greater suppression than in sim-

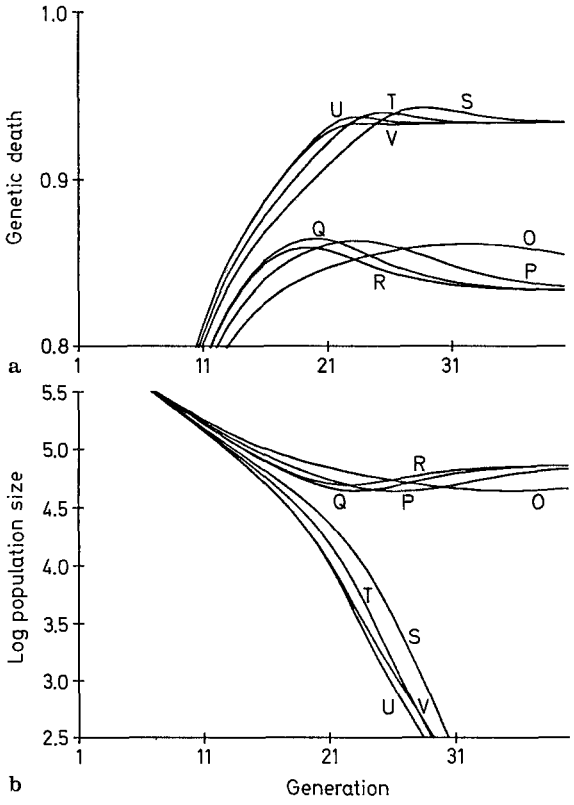

Fig. 4a and b. Simulations comparing SIT and FK strains containing two mutations within the inversion, with exchange between both mutations and the inversion break point (Type 3, Fig. 1c). Density-dependent populations; continuous releases 0.5 million per generation for 40 generations; A, F as in Fig. 2 legend; O, P, Q, R = translocation with inversion containing two mutations, exchange in region I = 0.333, 0.333, 0.333, 0.667, respectively, exchange in region III = 0.333, 0.667, 1.0, 0.667, respectively; S, T, U, V = translocation with inversion containing two mutations plus one unlinked mutation, exchange in region I = 0.333, 0.333, 0.333, 0.667, respectively, exchange in region III = 0.333, 0.667, 1.0, 0.667, respectively; exchange in region II = 1.0 for all inversions (see Table 1); **a** genetic death, **b** population size

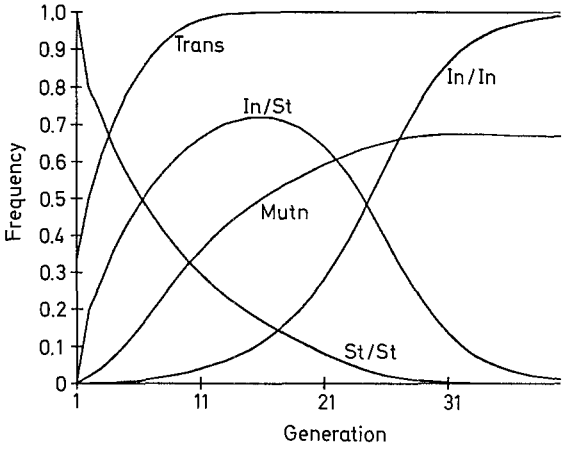

Fig. 5. Translocation, inversion, and mutation frequencies in simulation P from Fig. 4. Trans = translocation, In/St = inversion heterozygotes, In/In = inversion homozygotes, St/St = standard homozygotes, Mutn = mutation homozygotes

ilar strains with a single mutation, provided recombination within the inversion leads to genetic separation of the two mutations (simulations H–J, Fig. 3). This requires recombination both between the two mutations (region II, Fig. 1c) and between one inversion break point and one of the mutations (region III, Fig. 1c, in this example).

With two linked mutations and no exchange in region III (simulation G, Fig. 3), suppression is identical to the maximum possible with the single mutation only (simulation E, Fig. 2). With increasing exchange in region III, population suppression is greater (simulations H–J, Fig. 3). Eradication will eventually occur in simulations I and J.

Adding an unlinked mutation to the inversion strains described above greatly increases suppression, leading ultimately to eradication in all cases (simulations K–N, Fig. 3). Simulations J and K in this series (Fig. 3) gave nearly identical results to one another. Simulation K is equivalent to a FK/I strain with two mutations on heterologous chromosomes.

Importance of tight inversion-mutation linkage. The effect of recombination between the inversion and both mutations is illustrated in Fig. 4. In these simulations, the frequency of exchange varies in regions I and III (Type 3, Fig. 1c). With recombination in both regions, genetic death reaches a peak and then declines to an equilibrium level (Fig. 4a). Genetic death is initially higher in the simulations with higher recombination frequencies, reflecting higher homozygote frequencies, but declines earlier in these than in those with lower recombination.

The decline in genetic death results from a reduction in the frequency of female inversion heterozygotes, caused by displacement of the standard chromosome in the population by the inversion chromosome. The latter essentially becomes fixed in the female side of the population (Fig. 5).

The frequencies of mutation homozygotes and translocation and inversion karyotypes from simulation P (Fig. 4) are plotted in Fig. 5. Genetic death due to recombination within inversion heterozygotes was at a maximum in generations 15 and 16, when the heterozygote frequency was at a maximum (72%). Total genetic death in this simulation continued to rise for several generations after generation 16 (Fig. 4a), because the increasing frequency of homozygosis of mutations (Fig. 5) more than compensated for the decline in inversion heterozygote frequency until generation 24. Similar events occurred in the other two-mutation FK/I simulations, but earlier in simulations Q and R and later in simulation O (Fig. 4).

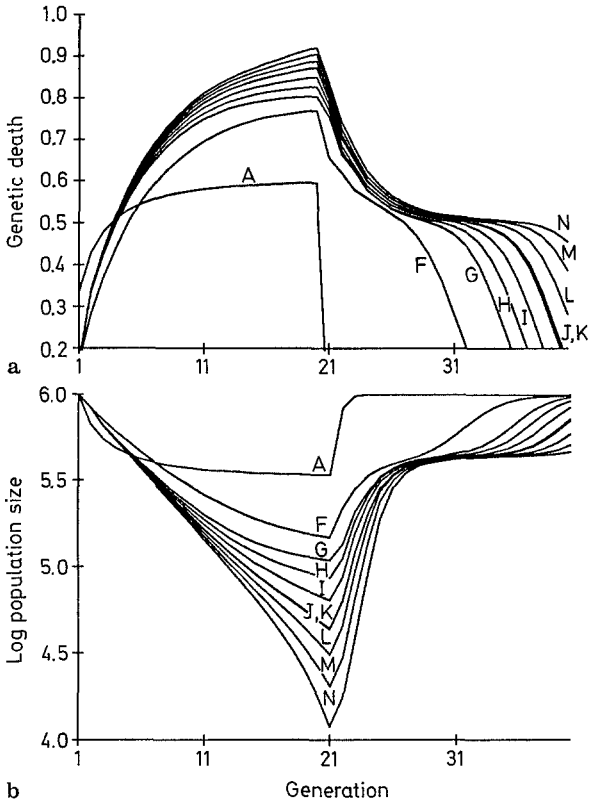

Fig. 6 a and b. Simulations comparing SIT and FK strains containing two mutations within the inversion, with at least one tightly linked to an inversion break point (Type 2, Fig. 1 c). Density-dependent populations; releases 0.5 million per generation ceasing after 20 generations; strains as in Fig. 3 legend or see Table 1; **a** genetic death, **b** population size

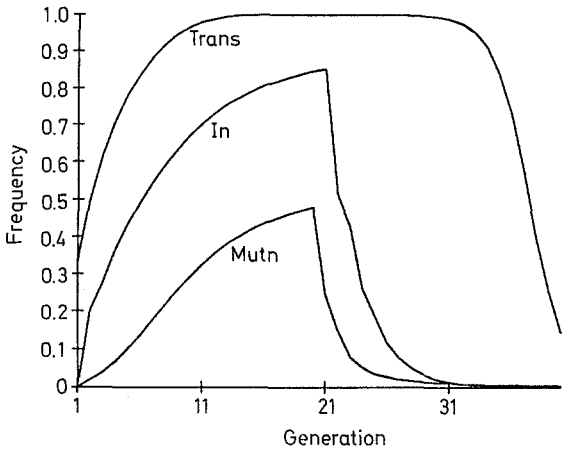

Fig. 7. Translocation, inversion, and mutation homozygote frequencies in simulation I from Fig. 6

Population size in simulation P began to increase in generation 27 (Fig. 4 b). The rate of genetic death in this and the other two-mutation simulations (O, Q, and R) declined to a level insufficient to overcome the density-dependent rate of population increase. In the three-mutation simulations (S, T, U, and V), the final rates of genetic death exceeded the value needed for eradication (90% in the case of $R_{MAX}=10$) (Fig. 4 a). These simulations were all near eradication at generation 40 (Fig. 4 b).

Interrupted releases. Persistence of genetic death and suppression following cessation of releases after 20 generations are illustrated in Fig. 6. The strains simulated in this series are identical to those used in the Fig. 3 series. The inversions significantly increase the duration of suppression after releases stop, compared to both sterile males and the FK/S strain.

Frequencies of translocations, inversion heterozygotes, and mutation homozygotes from simulation I (Fig. 6) are plotted in Fig. 7. The frequencies of the inversion and mutations rose more slowly than that of the translocation during the release phase and declined rapidly after releases ceased, accounting for the rapid initial decline in genetic death rates (Fig. 6 a). On the other hand, the translocation approached fixation in males rapidly, exceeding 99.9% in generation 16. Its frequency remained high for more than ten generations after releases stopped, giving continued population suppression during this period.

A similar pattern of genetic events occurred in the other simulations, but with near-fixation (in males) of the translocation occurring more slowly in simulations F–H and more rapidly in simulations J–N (Fig. 6). Since translocation and inversion sterilities were identical, the differences in genetic death rates among simulations G–N were due, in the first instance, to progressively increasing frequencies of mutation homozygosis. The increased suppression of native karyotypes caused by this increased genetic load thus led to more rapid increases in translocation and inversion frequencies.

Reduced maintenance releases. Simulations in which releases were not stopped altogether, but were lowered from 0.5 million to 0.2 million after 20 generations, are summarized in Fig. 8. This approach led to eradication in simulations M and N, at the expense of fewer released insects than the corresponding strains in Fig. 3. The other FK/I strain simulations (G–L) gave sufficient genetic death to sustain population suppression indefinitely to levels below 20% of the equilibrium population (10^6) (Fig. 8 b).

Density-influenced population regulation

Simulations using a constant release rate of 0.25 million males per generation against populations subject to density-influenced regulation are summarized in Fig. 9. The sterile males (simulation A) were the least effective at this release rate. The FK/S strain (simulation F) had suppressed peak population levels to below the starting pop-

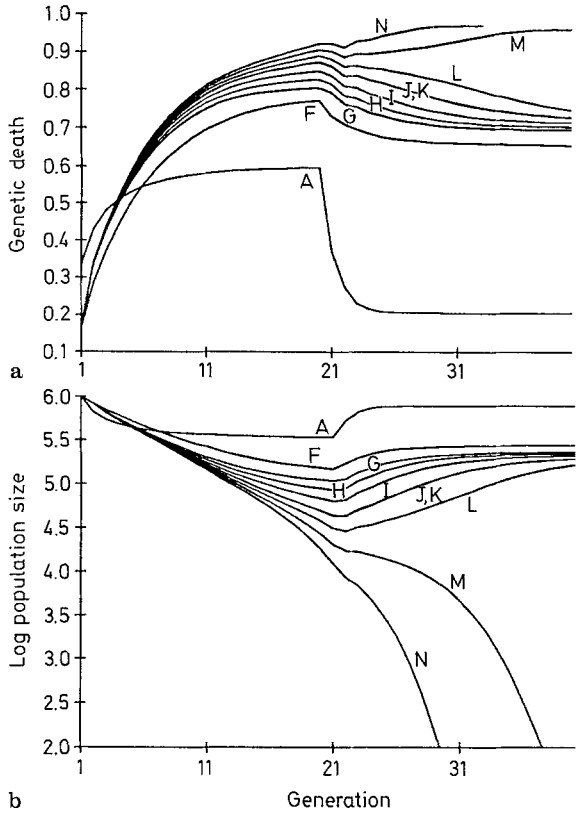

Fig. 8 a and b. Simulations comparing SIT and FK strains containing two mutations within the inversion, with at least one tightly linked to an inversion break point (Type 2, Fig. 1 c). Density-dependent populations; releases 0.5 million per generation for 20 generations, then 0.2 million per generation; strains as in Fig. 3 legend or see Table 1; **a** genetic death, **b** population size

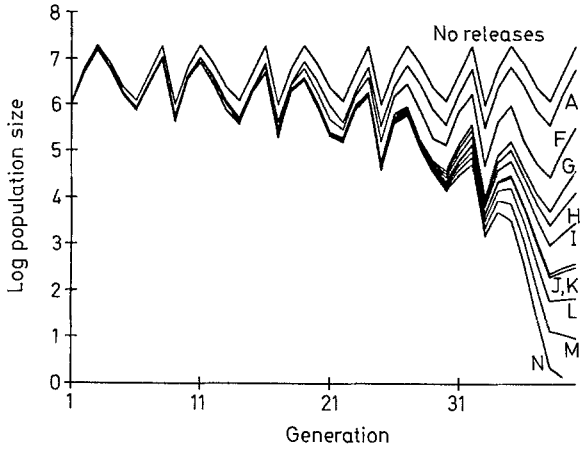

Fig. 9. Simulations comparing SIT and FK strains containing two mutations within the inversion, with at least one tightly linked to an inversion break point (Type 2, Fig. 1 c). Density-influenced populations; continuous releases 0.25 million per generation; strains as in Fig. 3 legend or see Table 1

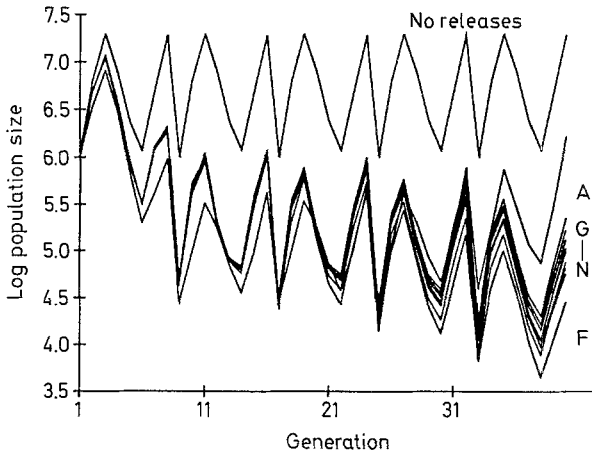

Fig. 10. Simulations comparing SIT and FK strains containing two mutations within the inversion, with at least one tightly linked to an inversion break point (Type 2, Fig. 1 c). Density-influenced populations; releases at high rate for first eight generations, then reduced for 32 generations, as detailed in Table 2; strains as in Fig. 3 legend or see Table 1

Table 2. Release rates for simulations in Fig. 10

Simulations	Release rate per generation (×1,000)		5-year total (×1,000)
	suppression phase	maintenance phase	
A	885	205	13,640
F	850	140	11,280
G	710	120	9,520
H	710	110	9,200
I	710	105	9,040
J	710	100	8,880
K, L	700	100	8,800
M, N	700	95	8,640

ulation level by the 5th year (generation 33 onward), while the FK/I strains (simulations G–N) achieved this milestone by the 4th year (generation 25 onward). Eradication occurred at generation 40 in simulation N. All the other FK-strain simulations would eventually produce eradication.

Simulations in which high release rates were used to suppress populations, followed by releases at lower rates to maintain the suppression, are illustrated in Fig. 10. The aim was to use combinations of two release rates sufficient (1) to achieve a tenfold population reduction by the end of the 1st year (eight generations), then (2) to maintain suppression so that the population peaks were restricted to approximately 10^6 individuals or less. The release numbers required to achieve the results shown in Fig. 10 are summarized in Table 2.

Discussion

The similarity of the results of simulations using either density-dependent populations (Fig. 3) or density-influenced populations (Fig. 8) supports the validity of the simple density-dependent model applied in most of the present and previous (Foster et al. 1988) simulations. Failure of sterile males at low release ratios to eradicate density-dependent/-influenced populations has also been reported in simulations of SIT control of *Dacus cucurbitae* (Ito and Koyama 1982). The present study and that of Ito and Koyama (1982) illustrate the importance of detailed ecological knowledge in evaluating the effects of SIT or other genetic techniques to control pest species.

The present simulations suggest that FK strains containing inversions have greater potential for population suppression than sterile males or presently available FK strains, especially at low release rates. The increased levels of genetic death in pericentric inversion heterozygotes are due to inviable products of exchange within the inverted segment. This kills up to half of the offspring of daughters of released males. Homozygosis of deleterious mutations in field-reared offspring remains an essential element of FK systems, however (Foster et al. 1988).

Both the initial rate of genetic death from FK strains and its persistence after cessation of releases are increased with inclusion of inversions (Fig. 6). This differs in detail from the situation arising from increased translocation sterility, which causes more rapid initial suppression but less persistence after releases stop (Foster et al. 1988).

Formally, the use of inversions in FK systems is similar to delayed sterility, in which release of fertile or partially sterile males produces progeny with increased sterility (Curtis 1968; Knipling 1970; Curtis and Hill 1971; Whitten 1971). The sterility in the case of higher Diptera is restricted to female offspring of released males, unlike systems involving translocations or systems with frequent meiotic recombination in both sexes.

The displacement of the standard chromosome by the inversion in simulations in which the white-eye mutation recombines with the inversion (Figs. 4 and 5) arises from the lower fertility of inversion/standard hybrids, and is similar to a situation predicted by Robinson (1975). When hybrids are less fit than both parent strains, there is an unstable equilibrium frequency for the two strains (Li 1955), at which they can theoretically coexist indefinitely. However, above or below this point, one or the other parent type will enjoy a selective advantage due to a higher frequency of successful matings and will eventually proceed to fixation (Curtis and Hill 1971; Whitten 1971; Foster et al. 1972).

In the present simulations, the released inversion-bearing chromosomes are inviable as homozygotes because they contain a deleterious mutation. However, with repeated release of mutation-bearing chromosomes accompanied by separation of the mutation and inversion, the frequency of inversion homozygotes eventually exceeds the unstable equilibrium frequency. The final (stable) equilibrium population size in simulations O–R (Fig. 4) is that expected from releasing a translocation strain containing no inversion and two mutations.

To avoid the decay in genetic death caused by displacement of standard chromosomes by inversions, the latter should be selected with at least one break point genetically close to the lethal mutant gene. This is especially important for long-term suppression programs. Even if genetic death is sufficient to cause eradication (e.g., simulations S–V, Fig. 4), recombination may delay this by several generations compared to similar strains with tighter mutation-inversion linkage (e.g., simulations M, N of Fig. 3).

Another property of pericentric inversions should also be borne in mind when selecting rearrangements for FK systems. Pericentric inversions that result in gross alteration of the ratio of the length of the long chromosome arm to that of the short arm exhibit a form of meiotic drive in heterozygous females. This is caused by differential recovery in the function egg nucleus of the shorter of a pair of unequal dyads (Novitski 1967), produced by exchange within inversion heterozygotes (Foster and Whitten 1974, 1991; Van Heemert 1977). The net effect is to favor recovery of the chromosome with the more centrally located centomere (Foster and Whitten 1991).

Thus, it would be advantageous to avoid inversions that displace the centromere to a more terminal position, since these would tend to be eliminated selectively by meiotic drive. Conversely, selecting inversions with more central centromeres would result in a tendency for meiotic drive to increase the frequency of inversion heterozygotes.

The results of simulations with variable release rates (Figs. 6, 8, 10) highlight the cost-saving potential and built-in safety margin of FK suppression systems compared to SIT releases. The inversions extend the period of protection following accidental or deliberate cessation of releases (Fig. 6) compared to noninversion FK systems (Foster et al. 1988).

In density-dependent populations, reducing the release rate by 60% after a 20-generation suppression phase almost completely negated suppression with SIT releases (Fig. 8). However, the FK strains gave prolonged suppression to much lower population sizes, ending with eradication in simulations M and N.

The results of the simulations with density-influenced populations (Fig. 10) suggest that a sequence of initial suppression for, e.g., 1 year at a high release rate, followed by a lower maintenance release rate, could give indefinite suppression to whatever level is desired. Assuming that suppression of the target population by an order of mag-

nitude represents economically beneficial pest control, these results suggest that FK strains could provide protection at a much lower cost than with SIT. The release numbers used for FK/I strains were 20–21% lower during the suppression phase and 41–54% lower during the maintenance phase than those required to achieve a similar result with SIT releases (Table 2). In a large-area rearing and release program, on-going savings of this order would represent several million dollars annually.

Acknowledgements. Research supported by grants from the Australian Wool Corporation.

References

Baker RH, Reisen WK, Sakai RK, Hayes CG, Aslamkhan M, Saifuddin UT, Mahmood F, Perveen A, Javed S (1979) Field assessment of mating competitiveness of male *Culex tritaeniorhynchus* carrying a complex chromosomal aberration. Ann Entomol Soc Am 72:751–758

Baker RH, Reisen WK, Sakai RK, Rathor HR, Raana K, Azra K, Niaz S (1980) *Anopheles culicifacies:* Mating behaviour and competitiveness in nature of males carrying a complex chromosomal aberration. Ann Entomol Soc Am 73:581–588

Busch-Petersen E (1989) Male recombination in a genetic sexing strain of *Ceratitis capitata* (Diptera: Tephritidae) and its effect on stability. Ann Entomol Soc Am 82:778–784

Curtis CF (1968) Possible use of translocations to fix desirable genes in insect pest populations. Nature 218:368–369

Curtis CF, Hill WG (1971) Theoretical studies on the use of translocations for the control of tsetse flies and other disease vectors. Theor Popul Biol 2:71–90

Curtis CF, Akiyama J, Davidson G (1976) A genetic sexing system in *Anopheles gambiae* species A. Mosq News 36:492–498

Dallwitz R, Roberts JA, Kitching RL (1984) Factors determining the predominance of *Lucilia cuprina* larvae in blowfly strikes of sheep in southern New South Wales. J Aust Entomol Soc 23:175–177

Foster GG (1989) The sheep blowfly genetic control program in Australia. FAO/IAEA Insect and Pest Control Newsletter, No. 43:23–26

Foster GG (1991) Chromosomal inversions and genetic control revisited: the use of inversions in sexing systems for higher Diptera. Theor Appl Genet 81:619–623

Foster GG, Smith PH (1991) Genetic control of *Lucilia cuprina:* analysis of field trial data using simulation techniques. Theor Appl Genet

Foster GG, Whitten MJ (1974) Unequal segregation in *Lucilia cuprina.* Genetics 77:s22–s23

Foster GG, Whitten MJ (1991) Meiotic drive in *Lucilia cuprina* and chromosomal evolution. Proc Conf Genet Biol Meiotic Drive, Honolulu, January 1988. Am Nat 137:403–415

Foster GG, Whitten MJ, Prout T, Gill R (1972) Chromosome rearrangements for the control of insect pests. Science 176: 875–880

Foster GG, Kitching RL, Vogt WG, Whitten MJ (1975) Sheep blowfly and its control in the pastoral ecosystem in Australia. Proc Ecol Soc Aust 9:213–229

Foster GG, Maddern RH, Mills AT (1980) Genetic instability in mass-rearing colonies of a sex-linked translocation strain of *Lucilia cuprina* (Wiedemann) (Diptera: Calliphoridae) during a field trial of genetic control. Theor Apl Genet 58:169–175

Foster GG, Whitten MJ, Konovalov C, Arnold JTA, Maffi G (1981) Autosomal genetic maps of the Australian sheep blowfly, *Lucilia cuprina dorsalis* R.-D. (Diptera: Calliphoridae), and possible correlations with the linkage groups of *Musca domestica* L. and *Drosophila melanogaster* (Mg.). Genet Res Camb 37:55–69

Foster GG, Vogt WG, Woodburn TL (1985) Genetic analysis of field trials of sex-linked translocation strains for genetic control of the Australian sheep blowfly *Lucilia cuprina* (Wiedemann). Aust J Biol Sci 38:275–293

Foster GG, Vogt WG, Woodburn TL, Smith PH (1988) Computer simulation of genetic control. Comparison of sterile males and field-female killing systems. Theor Appl Genet 76:870–879

Foster GG, Weller GL, Clarke GM (1991) Male crossing-over and genetic sexing systems in *Lucilia cuprina.* Heredity 67: (in press)

Hooper GHS, Robinson AS, Marchand RP (1987) Behaviour of a genetic sexing strain of Mediterranean fruit fly, *Ceratitis capitata,* during large-scale rearing. In: Fruit flies. Proc 2nd Int Symp, 16–21 September 1986, Colymbari, Crete, pp 349–362

Ito Y, Koyama J (1982) Eradication of the melon fly: role of population ecology in the successful implementation of the sterile insect release method. Prot Ecol 4:1–28

Kaiser PE, Seawright JA, Dame DA, Joslyn DJ (1978) Development of a genetic sexing system for *Anopheles albimanus.* J Econ Entomol 71:766–771

Kitching RL (1977) Time, resources and population dynamics in insects. Aust J Ecol 2:31–42

Knipling EF (1970) Suppression of pest Lepidoptera by releasing partially sterile males. A theoretical appraisal. Bio Science 20:465–470

Li CC (1955) The stability of an equilibrium and the average fitness of a population. Am Nat 89:281–296

Novitski E (1967) Nonrandom disjunction in Drosophila. Annu Rev Genetics 1:71–86

Prout T (1978) The joint effects of the release of sterile males and immigration of fertilized females on a density-regulated population. Theor Popul Biol 13:40–71

Robinson AS (1975) A reassessment of the use of chromosome inversions for insect control. J Hered 66:35–37

Robinson AS, Van Heemert C (1982) *Ceratitis capitata* – a suitable case for genetic sexing. Genetica 58:229–237

Rossler Y (1982a) Genetic recombination in males of the Mediterranean fruit fly and its relation to automated sexing methods. Ann Entomol Soc Am 75:28–31

Rossler Y (1982b) Recombination in males and females of the Mediterranean fruit fly (Diptera: Tephritidae), with and without chromosomal aberrations. Ann Entomol Soc Am 75:619–622

Stevens WL (1936) The analysis of interferrence. J Genet 32:51–64

Suguna SG, Seawright JA, Joslyn DJ, Rabbani MG (1981) Homozygous pericentric inversions and other studies of inversions on chromosome 3 in the mosquito *Anopheles albimanus.* Can J Genet Cytol 23:57–64

Tazima Y (1964) The genetics of the silkworm. Logos, London, 253 pages, pp 193–194

Van Heemert C (1977) Somatic pairing and meiotic nonrandom disjunction in a pericentric inversion of *Hylemya antiqua* (Meigen). Chromosoma 59:193–206

Vogt WG, Woodburn TL (1980) The influence of temperature and moisture on the survival and duration of the egg stage of the Australian sheep blowfly, *Lucilia cuprina* (Wiedemann) (Diptera: Calliphoridae). Bull Entomol Res 70:665–671

Vogt WG, Woodburn TL, Ellem BA, Van Gerwen ACM, Barton Browne L, Wardhaugh KG (1985a) The relationship be-

tween fecundity and oocyte resorption in field populations of *Lucilia cuprina*. Entomol Exp Appl 39:91–99

Vogt WG, Woodburn TL, Foster GG (1985b) Ecological analysis of field trials conducted to assess the potential of sex-linked translocation strains for genetic control of the Australian sheep blowfly, *Lucilia cuprina* (Wiedemann). Aust J Biol Sci 38:259–273

Whitten MJ (1969) Automated sexing of pupae and its usefulness in control by sterile insects. J Econ Entomol 62:272–273

Whitten MJ (1971) Insect control by genetic manipulation of natural populations. Science 171:682–684

Whitten MJ (1979) The use of genetically selected strains for pest replacement or suppression. In: Hoy MA, McKelvey JJ Jr (eds) Genetics in relation to insect management. The Rockefeller Foundation, New York, pp 31–40

Whitten MJ, Foster GG (1975) Genetical methods of pest control. Annu Rev Entomol 20:461–476

Whitten MJ, Foster GG, Vogt WG, Kitching RL, Woodburn TL, Konovalov C (1977) Current status of genetic control of the Australian sheep blowfly, *Lucilia cuprina* (Wiedemann) (Diptera: Calliphoridae). Proc 15th Int Congr Entomol, Washington, D.C., 1976, pp 129–139