1 Title: Optimal control in the face of evolving resistance by hiding portions of the popu-

2 lation from selection.

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4 Childs

# 5 Introduction

6 Controlling populations in the face evolving resistance to xenobiotics (i.e. antibiotics,

7 herbicides, pesticides, fungicides) is one of the biggest challenges facing public health

8 [(Laxminarayan *et al.*](#_bookmark31), [2016;](#_bookmark31) [Willyard *et al.*](#_bookmark48), [2017),](#_bookmark48) and food security [(Denholm & Row-](#_bookmark22)

9 [land,](#_bookmark22) [1992;](#_bookmark22) [Palumbi,](#_bookmark37) [2001;](#_bookmark37) [Hicks *et al.*](#_bookmark29), [2018).](#_bookmark29) Evolved resistance also costs billions of

10 dollars globally [(Livingston *et al.*](#_bookmark32), [2016;](#_bookmark32) [Chesson *et al.*](#_bookmark17), [2018;](#_bookmark17) [Hicks *et al.*](#_bookmark29), [2018).](#_bookmark29) While

11 there have been some successes in combating resistance in public health [(REX Consor-](#_bookmark41)

12 [tium, 2013),](#_bookmark41) resistance is still a major problem in health care [(Willyard *et al.*](#_bookmark48), [2017)](#_bookmark48) and

13 there has been little success in other contexts, such as food production.

14 Current strategies to manage resistance focus on delaying the initial evolution of re-

15 sistance by reducing the population (reducing the potential for *de nova* resistance mu-

16 tations), and killing any resistant mutants by using a second compound [(Denholm &](#_bookmark22)

17 [Rowland, 1992;](#_bookmark22) [REX Consortium, 2013)](#_bookmark41). Multiple compounds are either stacked (used at

18 the same time) or cycled in sequence. While these strategies can be effective in delaying

19 the initial evolution of resistance they may be counter-productive if xenobiotic resistance

20 is already present, which is true of important pests of food production systems [(Den-](#_bookmark22)

21 [holm & Rowland, 1992;](#_bookmark22) [Hicks *et al.*](#_bookmark29), [2018)](#_bookmark29) and threats to human health [(Willyard *et al.*](#_bookmark48),

22 [2017).](#_bookmark48) Strategies like stacking and cycling involve the continuous (and even increased)

23 use of xenobiotics, which can help drive existing resistance through an entire population

24 [(Denholm & Rowland, 1992](#_bookmark22); [Hicks *et al.*](#_bookmark29), [2018).](#_bookmark29)

25 In agricultural systems an alternative once resistance has evolved is integrated pest man-

26 agement (IPM), where chemical control is used in combination with non-chemical control

27 such as crop rotation, cultivation and spot control (which can involve broad spectrum

28 xenobiotics or mechanical control). While the concept of integrated pest management is

29 well established [(Bottrell *et al.*](#_bookmark11), [1979),](#_bookmark11) finding good IPM strategies is challenging [(Dana](#_bookmark21)

30 [*et al.*](#_bookmark21), [2014;](#_bookmark21) [Chalak & Pannell, 2015).](#_bookmark16) Management tools need to be used in the correct

31 combination and sequence to be most effective. This results in a very large number of po-

32 tential IPM strategies (i.e. different combinations and sequences), even when considering

33 only a handful of management tools and short time horizons (C[halak & Pannell, 2015).](#_bookmark16)

34 As a result there have been few attempts to rigorously search for good IPM strategies (see

35 [Chalak & Pannell 2015](#_bookmark16) for an exception). More commonly optimal strategies have looked

36 for the best allocation between a few management options ([Epanchin-Niell & Hastings,](#_bookmark24)

37 [2010;](#_bookmark24) [Meisner *et al.*](#_bookmark34), [2016;](#_bookmark34) [Okumura *et al.*](#_bookmark36), [2016;](#_bookmark36) [Bu¨yu¨ktahtakın & Haigh](#_bookmark12)t, [2017),](#_bookmark12) and

38 none have been developed where resistance could evolve to one of the primary manage-

39 ment tools. These are important omissions for food production systems where resistance

40 to xenobiotics has evolved numerous times [(Denholm & Rowland, 1992;](#_bookmark22) [Palumbi, 2001)](#_bookmark37)

41 and multiple non-chemical control options are available that can used in combination to

42 deliver cost effective control [(Chalak & Pannell, 2015).](#_bookmark16)

43 Little is known about how robust good IPM strategies are to changes in factors such as

44 crop yield and pest population dynamics [(Epanchin-Niell & Hastings,](#_bookmark24) [2010).](#_bookmark24) However,

45 previous work on the optimal control of invasive populations has found general factors that

46 shape optimal decisions. Biologically, a population’s ability to escape density dependence

47 shifts optimal control to younger age classes [(Pichancourt *et al.*](#_bookmark38), [2012).](#_bookmark38) The degree to

48 which eradicated regions can be re-invaded also influences the optimal control strategies

49 [(Januchowski-Hartley *et al.*](#_bookmark30), [2011;](#_bookmark30) [Epanchin-Niell & Wilen, 2012),](#_bookmark25) but the exact strategy

50 depends on the way suitable habitats are connected [(Chad`es *et al.*](#_bookmark15), [2011).](#_bookmark15) Economic

51 factors tend to be at least as important as biological ones in shaping the optimal con-

52 trol strategy [(Epanchin-Niell & Hastings,](#_bookmark24) [2010).](#_bookmark24) In particular the relationship between

53 the density of an invasive species and the damage it does has been found to be crucial

54 (Y[okomizo *et al.*](#_bookmark49), [2009).](#_bookmark49) The way that future returns are valued also strongly influences

55 the optimal control strategy, when more value is placed on future versus present returns

56 more intensive control is favoured [(Epanchin-Niell & Hastings, 2010).](#_bookmark24)

57 We apply a genetic algorithm to a model of resistance to two herbicides in an important

58 weed of wheat in Europe (*Alopecurus myosuroides*). [ALEXA: sentence or two here +

59 REF on just how damaging BG is]. To allow IPM strategies we also include crop rotation,

60 cultivation and spot control as management options. We find that good IPM strategies are

61 highly context dependent, with crop yields, the yield penalty imposed by the weed, and

62 parameters which control how large the population can grow, having the most influence

63 on what makes a good IPM strategy.

64 **Methods**

65 We frame IPM as a combinatorial optimisation problem where the goal is to find a good

66 combination of management tools, used in sequence. We use a genetic algorithm to solve

67 this combinatorial problem (T[aylor & Hastings,](#_bookmark44) [2004;](#_bookmark44) [Carrasco *et al.*](#_bookmark13), [2010).](#_bookmark13) Genetic

68 algorithms cannot be checked to have found the globally optimal solution, as this would

69 require already knowing the solution. However, genetic algorithms are efficient at weeding

70 out comparatively poor solutions, so that over successive iterations the regions of the

71 solution space being explored gets progressively better, resulting in a set of good (often

72 near optimal) solutions.

73 Our goal is to find good IPM strategies in the face of rapidly evolving resistance, and

74 how those strategies change in response to biological and management parameters. This

75 problem has fours parts: i) A reward function that measures how good a given IPM

76 strategy is based on how much that strategy cost and its effectiveness, we use net present

77 economic value. ii) A population model that translates a given IPM strategy into a

78 population, and thus a reward. iii) An algorithm that finds IPM strategies with higher

79 rewards, the genetic algorithm. iv) Finally we need to relate changes in the best IPM

80 strategy found to changes in initial conditions and model parameters. We use a meta-

81 modelling global sensitivity analysis [(Coutts & Yokomizo,](#_bookmark20) [2014)](#_bookmark20) based on multi-variate

82 boosted regression trees [(Miller *et al.*](#_bookmark35), [2016).](#_bookmark35)

## 83 Population model

84 The population model links management actions to the response of the *A. myosuroides*

85 population, and thus wheat yields. The action a*j* is how the manager effects the popu-

86 lation model, and thus the reward they get. Each action is a tuple of four sub-actions

87 a*j* = (a*h*, a*b*, a*k*, a*s*), see [Appendix 1](#_bookmark6) for a description of the sub-actions and all eligible

88 combinations of these sub-actions (i.e. the full actions space, **A**).

89 The processes included in the population model limit the scope of the IPM strategies

90 found. We use a deterministic model, and so our IPM strategies can only deal with average

91 expected population responses, ignoring demographic uncertainty, and environmental and

92 market variability. Also, we only model herbicide resistance that is already present in the

93 population because *de nova* mutation is a fundamentally stochastic process.

94 A commonly recommended [(REX Consortium,](#_bookmark41) [2013)](#_bookmark41) and applied [(Hicks *et al.*](#_bookmark29), [2018)](#_bookmark29)

95 strategy to combat resistance is to apply xenobiotics that impair different cellar pathways

96 (i.e. modes of action), either sequentially (cycling) or concurrently (stacking). To allow

97 this behaviour we use a discrete time, spatially implicit model, where two independent

98 alleles (R and Q), each confer target site resistance to a separate herbicide. The model

99 must also be flexible enough to accommodate non-chemical control. We include a two

100 level seed bank (to allow plowing to take seeds out of the germinating population) and

101 model survival as a function of resistance, herbicide choice, crop choice and spot control

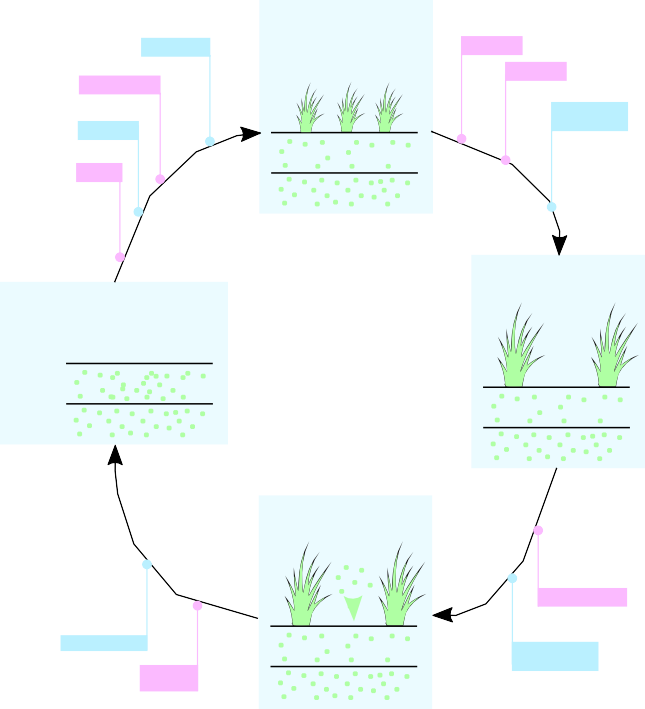
102 (where the cost increases with *A. myosuroides* density).

103 We model the *A. myosuroides* population using a yearly time step, starting at the begin-

104 ning of the growing season before any seeds have emerged. See Figure [1](#_bookmark0) for the timing

105 of management interventions and [Appendix 2](#_bookmark7) for a full description of the model and how

106 each sub-action affects the population.



Above ground

n(**G**, t)

germination

herbicide 1

herbicide 2

crop choice (k)

survival

s(**G**, ah, ak, t)

b'(**G**, ab, t)

plowing

Survivors

n'(**G**, t)

Seed bank

top level b(**G**, 1, t)

lower level b(**G**, 2, t)

Seed production

**f**(t)

spot control (as)

seed mortality

flowering and parent crossing

Reward calculated

Figure 1: Life cycle with management interventions over the year. Pink processes are management interventions and blue processes are biological population processes.

107 **Reward function**

108 The reward function measures how good an IPM strategy is, given a initial starting

109 condition and parameter set that the model is run under. The reward function encodes

110 the goals of a manager. We assume farmers are primarily driven by economic returns.

111 The economic return consists of two parts, the income made from the crop and the costs of

112 producing that crop. We assume that usual farm costs, such as buildings and machinery

113 as constant from year to year, so we focus on gross margin, i.e. income - variable costs

114 [(Redman, 2016,](#_bookmark40) pp. 3–4).

115 To explicitly link the above ground population to the reward function we define N *jj*(**a**, n0, t),

116 the total above ground population after all control actions, at time t given an initial pop-

117 ulation n0 and a sequence of actions

0 1 *T*

118 **a** = {a*j* , a*j* , · · · , a*j* } (1)

119 where a*t* is the action a*j* ∈ **A** taken at time t and T is the time horizon over which

*j*

120 management is run. We assume all returns after T are ignored. The reward function is

121

R(**a**, n0) =

*T*

Σ*t*=0

γ*t*.

Y (N *jj*(**a**, n0, t)) − C(a*t* )Σ

(2)

122 where R(**a**, n0) is the time discounted reward for action sequence **a** given starting popu-

*j*

123 lation n0, γ ∈ [0, 1] is the discount rate. When γ = 0 only the reward in the first time

124 step is considered, when γ = 1 returns in all future time steps up to T are valued equally.

125 Y (N *jj*(**a**, n0, t)) is the income (in £/ha) from the crop chosen at time t given start stating

126 n0 and following action sequence **a**. C(a*j*) is the cost of taking action a*j*, and is composed

127 of the cost of controlling *A. myosuroides* and other costs that depend in the crop being

128 grown (a*k*).

129 See [Appendix 3](#_bookmark8) for the yield and cost models for each sub-action and parameter estima-

130 tion.

## 131 Finding good IPM strategies

132 Our goal is to find good strategists to manage black grass in the face of evolving resistance,

133 however it is not feasible to test every combination of management options over more than

134 a handful of years. Genetic algorithms have been used to find good solutions to this class

135 of problem (T[aylor & Hastings, 2004;](#_bookmark44) [Carrasco *et al.*](#_bookmark13), [2010).](#_bookmark13) The genetic algorithm starts

136 with an randomly generated set of action sequences, these action sequences are then

137 iteratively improved to find a set of action sequences with a high gross margin. Genetic

138 algorithms rely on the fact that even though the number of possible action sequences

139 is large, many perform very poorly. The genetic algorithm explores better performing

140 regions of the solution space more intensely. While genetic algorithms are not guaranteed

141 to find the optimal action sequence they will find a set of actions sequences that perform

142 well, often close to the optimal solution.

143 To find good action sequences we use a genetic algorithm with knock out tournament

144 selection, where each action sequence in a set of 1000 actions sequences is randomly

145 paired with another, and the action sequence with the highest R(**a**, n0) survives to help

146 generate new action sequences. We used pair mating between survivors and N-point cross-

147 over to produce new action sequences. After new action sequences are created there is a

*t t*

148 process of random mutation where each a*j* is changed to another a*j* ∈ **A** with probability

149 m = 0.03. The algorithm used is given in [Appendix 4.](#_bookmark9)

## 150 Finding which initial conditions and model parameters lead to

151 **which IPM strategies**

152 It is unlikely a given IPM strategy will perform well in all scenarios. To find the parameters

153 and initial conditions (n0) that shaped the IPM strategy with the highest reward, we

154 extend the meta-modelling approach to global sensitivity analysis outlined in [Coutts &](#_bookmark20)

155 [Yokomizo (2014),](#_bookmark20) to multivariate time series outputs (i.e. the sequences of the four sub

156 actions). We: i) ran the genetic algorithm under 15000 different parameter sets and initial

157 conditions, generated with Latin hyper-cube sampling (see Table [1](#_bookmark1) for upper and lower

158 limits of each parameter), ii) used Longest Common Sub-Sequence (T[oohey,](#_bookmark46) [201](#_bookmark46)5) as a

159 measure of distance between these action sequences, iii) projected the resulting distance

160 matrix into an 8D solution space using non-metric multi-dimensional scaling (implemented

161 in the ’ecodist’ R package; [Goslee & Urban 2007),](#_bookmark27) iv) predicted where each IPM solution

162 sat in the solution space using multi-variate boosted regression tree [(Miller *et al.*](#_bookmark35), [201](#_bookmark35)6),

163 where the model parameters and initial conditions were predictors. See [Appendix 5](#_bookmark10) for

164 details.

165 It was this multi-variate boosted regression tree we interrogated to find which parameters

166 and initial conditions were important for changing the best IPM strategy found–using

167 relative influence and partial dependence plots ([Miller *et al.*](#_bookmark35), [2016).](#_bookmark35)

Table 1: Parameter descriptions and the range each parameter was tested over

### Para- meter

**Units Range Description Source**

*Population Model see* [*Appendix 2*](#_bookmark7)

φ*e* prob. 0.45–0.6 germination probability [Colbach *et al.* (2006)](#_bookmark18)

φ*b* prob. 0.2–0.86 Probability a seed survives

one year

s0 prob. fixed 0.99 Survival probability with-

out herbicide

[Colbach *et al.*](#_bookmark18)[(2006),](#_bookmark18) [Thompson *et al.*](#_bookmark45)[(1997),](#_bookmark45) [Cavan *et al.*](#_bookmark14)[(1999)](#_bookmark14)

Assumed fixed and high so density ef- fects only expressed through fecundity.

θ prob. 0.7–1 Proportion of *A. myosuroides* population exposed

to herbicide under sub-action a*h* = herb R, herb Q or both. plants may be missed spatially or tempo- rally, or spraying may be affected by rain. Tested over wide range.

s*h* prob. 0.01 Survival of susceptible *A.*

*myosuroides* exposed to herbicide (a*h*

α prob. 0.22–0.04 Survival probability under

the alternative crop (a*k* = alt), spring barley.

β prob. 0.05–0.2 Survival under spot control

(sub-action a*s*), for example because plants are missed

herbicide assumed to be effective.

[Lutman *et al.* (2013)](#_bookmark33)

tested over wide range.

f*m* seeds· plant*−*1

30–300 Number of seeds produced when density is 0 (f*m*) and The effect of density on seed production (f*d*) interact to determine maximum population size.

Values chosen to keep the max population close to the maximum population seen in [Queenborough](#_bookmark39)

Table 1: Parameter descriptions and the range each parameter was tested over

### Para- meter

**Units Range Description Source**

f*d* 1

*plants·ha−*1

0.001–0.0001

I prob. 0.5–0.9 The proportion of seed

moved between seed bank levels by ploughing (sub- action a*b*)

[Grundy *et al.* (1999)](#_bookmark28)

*Reward function see* [*Appendix 3*](#_bookmark8)

γ 0.75–1 discount rate on future re- turns

Y0 £·ha*−*1 968–1758 Yield from winter wheat

when *A. myosuroides* is ab- sent.

tested over wide range

Upper limit upper 95% confidence inter- val from fitted yield function [(Appendix](#_bookmark8) [3).](#_bookmark8) Lower limit from low production sce- nario [Redman](#_bookmark40) [(2016,](#_bookmark40)

pp. 9).

Y*D* £·plant·

ha*−*1

0.0002–0.006 reduction in yield cuased by

each *A. myosuroides*.

95% confidence in- terval from fitted yield function, see [Appendix 3.](#_bookmark8)

Table 1: Parameter descriptions and the range each parameter was tested over

### Para-

**Units Range Description Source**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **meter** |  | | | |
| ϑ | £·ha*−*1 | 672–920 | Yield of spring barley,  an alternative crop com- | [Redman](#_bookmark40) [(2016,](#_bookmark40)  pp. 12) |
|  |  |  | monly used to control *A.* |  |
|  |  |  | *myosuroides*. |  |
| α | prop. | 0.85–1 | proportion of yield achieved | [Redman (2016,](#_bookmark40) pp. 9) |
|  |  |  | if crop a*k* is repeated |  |
| η*h* | £·ha*−*1 | 50–100 | Cost of a single herbicide  application | [Redman (2016,](#_bookmark40) pp. 9) |
| η*b* | £·ha*−*1 | 55–92 | Cost of ploughing | [Redman](#_bookmark40) [(2016,](#_bookmark40)  pp. 202) |

0 £·ha*−*1 10–100 Cost of spot control even

η

*s*

when *A. myosuroides* den- sity is 0

tested over wide range

η*s* £·plant. ha*−*1

10–100 Increase in spot control cost

for each *A. myosuroides*

tested over wide range

ηwheat £·ha*−*1 383 Cost of growing winter

wheat not associated with

1. *myosuroides* control

ηalt £·ha*−*1 273 Cost of growing the alterna-

tive crop, spring barley.

ηfal £·ha*−*1 36 Cost of a fallow rota-

tion. Based on two ap- plications of glyphosate to control any germinating *A. myosuroides*.

[Redman (2016,](#_bookmark40) pp. 9)

[Redman](#_bookmark40) [(2016,](#_bookmark40)

pp. 12)

[Redman](#_bookmark40) [(2016,](#_bookmark40)

pp. 202 and 284)

*Initial Conditions*

Table 1: Parameter descriptions and the range each parameter was tested over

### Para-

|  |  |  |  |
| --- | --- | --- | --- |
| **meter** | **Units** | **Range** | **Description Source** |
| Rint Qint Nint |  | 0–1  0–1  100–  100000 | Initial frequency of R alleles Initial frequency of Q alleles Initial number of seeds in  each level of the seed bank |

168 **Results**

169 IPM strategies with high gross margins were dependent on the yield of winter wheat (Y0),

170 the slope of the yield function (Y*D*) and a set of parameters that control how large the seed

171 bank can become, f*max*, f*d* and φ*b* (Figure [2)](#_bookmark2). Discount rate (γ), initial resistance to the

172 most effective herbicide, and the cost and effectiveness of spot control, all had moderate

173 effects on at least two dimensions. There are some interesting exclusions from this list.

174 Despite plowing forming a part of many good IPM strategies its cost and effectiveness

175 have very little influence on how it is used. This suggests that if it is a good idea to plow,

176 it is worth doing regardless of the cost and how much of the seed bank it inverts (at least

177 within the limits we tested). *A prior* we had thought that the initial population would

178 have a large effect on the structure of a good IPM strategy, since weed control at very high

179 population densities often looks very different to managing small populations. However

180 our analysis suggests that initial population size had very little relative influence. If other

181 parameters are such that effective control is possible even large seed banks can be quickly

182 reduced, and if they are not small populations can quickly grow to large ones.

183 We examine how these key parameters change the structure of IPM strategies with high

184 gross margin. We plot the effect in combinations since interactions between parameters

185 are important.

Y\_slope fec\_dd

Y0

fec\_max seed\_sur int\_G\_min dis\_rate spot\_fix sur\_spot

parameter

Y\_alt rep\_pen int\_G\_max

int\_N p\_ex cost\_herb inv\_frac cost\_plow spot\_var sur\_alt germ\_prob

17.6 16.9 10.6 18.6 11.3 12 33.1 11.6

18.5 11.7 7.4 10.8 8.6 13.5 18.3 15.2

6.3 10.6 30.6 11.3 8.2 3.2 2.8 8.3

6.1 10.6 9.7 11.5 8.5 5.6 18.2 3.1

6 7.9 11 8.7 7.5 9.9 8.6 5.3

4.9 5.7 3.7 5.6 9.7 7.6 2.8 3.3

5.1 3.8 2.4 3 5.5 8.4 2.3 6.9

7 2.6 2.1 2.3 2.8 8.6 2.5 7.7

7.7 2.8 2.9 2.1 2.8 7.9 2 7.1

2.1 3.4 5.7 3.5 3 1.4 1.1 3.1

1.6 3.3 5.5 3.1 3.2 2.1 0.9 3.3

2.4 2.9 1.1 3 5.6 2.4 1.1 3.6

2.8 2.4 1.3 2.3 3.3 3.7 0.8 4.1

1.7 2.5 1.2 2.4 3.1 4 0.8 3.1

1.8 2.7 2.6 3.2 2.1 1.1 2.5

2.6 2.1 0.8 2.3 4.1 1.5 2.5

1.7 1.7 0.8 2 3.5 1.5 2.2

1.4 2.1 1.7 2.1 1.7 2.7

1.3 2.2 0.9 1.6 2 1.4 2.4

1.3 1.8 0.8 1.7 2.1 1.5 2

D1 D2 D3 D4 D5 D6 D7 D8

NMDS dimention

Figure 2: Relative influence (relative reduction in squared error [mvtb REF]) of each parameter. Values are scaled 0 to 100, with higher values indicating parameters (rows) that had more influence on where solutions sat in each dimension of the solution space (columns). Parameters could have a larger effect on the structure of a good IMP strategy by either being very influential in one dimension (e.g. Y0), or having moderate influence across several dimensions (e.g. f*d*).

186 When the slope of the yield function (Y*D*) was low the best IPM strategy found was to

187 do nothing, as the yield penalty incurred by even high densities of *A. myosuroides* did

188 not incur a large enough cost to justify spending on control (although crop rotation was

189 carried out when the yields of winter wheat were low. This was true across a wide range

190 of values for other parameters.

191 When the slope of the yield function was high, and winter wheat yield decreased sharply

192 with increasing *A. myosuroides* density, a wider range of IPM strategies were found

193 (Figure [3).](#_bookmark3) When winter wheat yields were high (Figure [3a,b)](#_bookmark3) IPM strategies centred

194 on growing winter wheat, and using intensive management to reduce the density of *A.*

195 *myosuroides*. When at least one effective herbicide was available this involved all non-crop

196 options (Figure [3b).](#_bookmark3) When there was no effective herbicide (due to high initial levels of

197 resistance) plowing was the only action used to try and control the seed bank. When win-

198 ter wheat yields were low (Figure [3c,d),](#_bookmark3) spring crop dominated rotations and spot control

199 were favored, with more tactical use of herbicide when at least one effective compound was available [(3d).](#_bookmark3)

spot a) plow herb crop

int res min  0.9

spot c) plow herb crop

b)

d)

int res min  1e−04

1 4 7 10 1 4 7 10

time step

sub−actions herb R winter wheat spring crop plowed

spot control none

Y0 high

Y0 low

Figure 3: The good IPM strategies under high (£1668·ha*−*1) and low (£986·ha*−*1) values of Y0 (yield of winter wheat with no *A. myosuroides*). The left column shows IPM strategy when there is high initial resistance to both herbicides and the right column shows IPM strategy when initial resistance to one herbicide is low. The effect of *A. myosuroides* density on winter wheat yield (Y*D*) is 0.0062 £ plant*−*1 ha*−*1. Low values of Y*D* lead to no control being the best IPM strategy.

· ·

200

201 Intensive management to reduce the seed bank was only used when discount rates were

202 high (Figure [4).](#_bookmark4) Recall that although we only show the first 10 years of IPM strategy,

203 the discounted returns over 25 years are considered by the genetic algorithm. With low

204 winter wheat yields, high *A. myosuroides* seed banks were managed by cycling herbicides

205 to reduce the above ground population, and alternating winter wheat and spring crops.

206 In order to reduce the seed bank spot control was needed post plowing and herbicide to

207 keep the seed producing population of *A. myosuroides* very low.

208 When both herbicides were effective the preference was to cycle between them, however

209 even this did not prolong their continued use by much. Even when both R and Q started

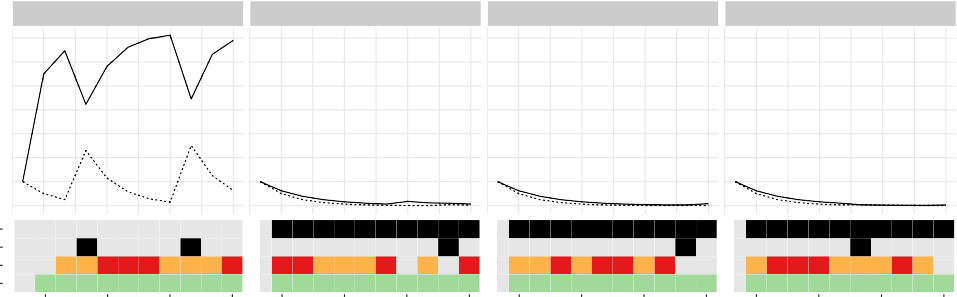
210 at frequencies of 1 in 20,000 alleles (Figure [5a)](#_bookmark5) continued herbicide use raised those fre-

211 quencies to 1 in 50 within 10 time steps. This frequency provided enough variation for

212 selection to rapidly act on (Figure [5c).](#_bookmark5)

213 Even when initial frequencies of resistance to the remaining effective herbicide was low (1

214 in 200; Figure [5c)](#_bookmark5) initial continual use quickly drove the evolution of resistance to levels

a)

  0.75

number seeds (x1000)

300

200

100



0

spot

  

  1

  0.83









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  0.92



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

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seed bank level







SB1

 SB2

sub−actions

herb 1

herb 2

plow herb crop







1 4 7 10

1 4 7 10

1 4 7 10

1 4 7 10

winter wheat spring crop plowed

spot control

b)

number seeds (x1000)

300



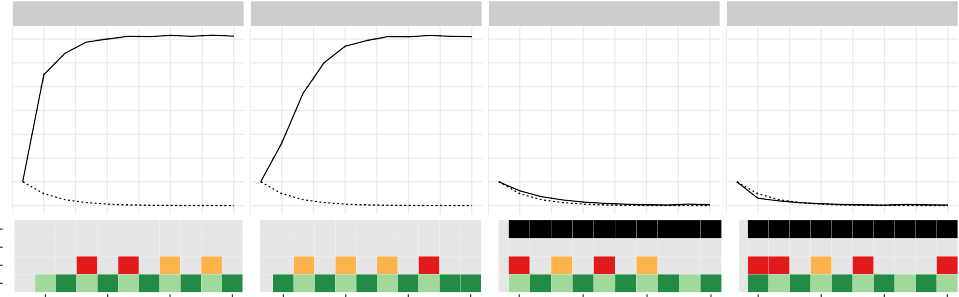
       



time step

  0.83

  1

     



  0.92

  0.75



none

200



100







0

spot plow herb crop







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1 4 7 10

1 4 7 10

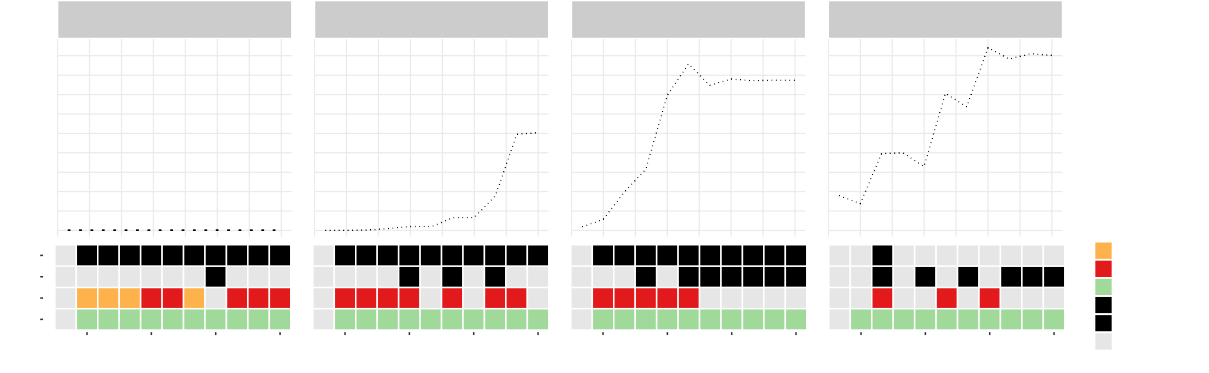
1 4 7 10

1 4 7 10

time step

Figure 4: The effect of discount rate (γ) on the seed bank and IPM strategy (tile plots) when yields from winter wheat are high (a) and low (b). In both cases the slope of the yield function (Y*D*) is high, with a large effect of *A. myosuroides*. Initial resistance was low for both herbicides.

a)



int %R = 5e−05 int %Q = 5e−05

sur. under both herb.

0.4

0.3

0.2

0.1

b) c)





int %R = 0.45 int %Q = 0.005

int %R = 0.45 int %Q = 5e−05

 







d) 





 

 











int %R = 0.45 int %Q = 0.05

  

reward (£)

1100

1000

900

800

700

0.0

spot plow herb crop





 



 



          

sub−actions herb R herb Q

winter wheat plowed

spot control

1 4 7 10 1 4 7 10 1 4 7 10 1 4 7 10

time step

none

Figure 5: The effect of initial resistance on the selected IPM strategy (tile plots) and the evolution of herbicide resistance (% survival to under both herbicides). Lighter coloured points indicate higher reward (gross margin) obtained in that time step. In this case Y0 = 1668 (high winter wheat yield) and Y*D* = 0.0062 (high yield penalty).

215 where herbicide use was greatly reduced after just five generations. As the initial frequency

216 of resistance to the remaining effective herbicide (’herb Q’ in this case) increased, even

217 moderate herbicide use drove the rapid evolution of herbicide resistance. With an initial

218 frequency of resistance alleles of 1 in 20 even three herbicide applications were enough

219 to increase resistance to the point where applying both herbicides would result in 40%

220 survival (Figure [5d).](#_bookmark5) Once this situation was reached, gross margin was reduced

221 quarter compared to returns with low resistance.

222 **Discussion**

223 We found that IPM strategies were highly dependent on the yield function, relating the

224 density of *A. myosuroides* to winter wheat yields, and the density that *A. myosuroides*

225 could reach (which interacts with the yield function). To a lesser extent IPM strategies

226 were shaped by the way future returns were valued and the initial frequency of herbicide

227 resistance in the population. The IPM strategies with the best returns ranged from doing

228 nothing, to high intensity management.

229 Herbicide use was greatly reduced when even moderate resistance evolved, which could

230 happen after as few as five generations exposed to herbicide. This is in contrast to current

231 management practice in this cropping system, where multiple herbicide applications a year

232 are the norm, despite high levels of resistance [(Hicks *et al.*](#_bookmark29), [2018).](#_bookmark29) [HELEN: Could you

233 flesh this out a bit by suggesting a few reasons why the difference, and cost of using

234 ineffective herbicides]

235 The key uncertainties highlighted by this work were economic. It is not surprising that

236 economic factors shaped IPM strategies. Factors such as crop prices, harvest efficiency

237 and costs, directly affect the gross margin of an IPM strategy. Although yield functions

238 have been estimated for major weeds [(Cousens, 1985;](#_bookmark19) [Doyle *et al.*](#_bookmark23), [1986;](#_bookmark23) [Swinton *et al.*](#_bookmark43),

239 [1994),](#_bookmark43) there is evidence that yield functions vary substantially between fields [(Swinton](#_bookmark43)

240 [*et al.*](#_bookmark43), [1994;](#_bookmark43) [Hicks *et al.*](#_bookmark29), [2018),](#_bookmark29) and little attention has been paid this variation and under-

241 standing its causes. This poses a considerable challenge for formulating IPM strategies,

242 as what works well in one field may not be transferable to another.

243 Supporting previous work [(Epanchin-Niell & Hastings, 2010)](#_bookmark24) we found higher values on

244 future returns lead to more intensive IPM strategies. In agricultural systems those who

245 own fields can benefit from long-term investments like weed control campaigns and soil

246 conservation, whereas those who rent fields do not [(Wiese *et al.*](#_bookmark47), [1996;](#_bookmark47) [Fraser](#_bookmark26), [2004).](#_bookmark26)

247 [HELEN/ALEXA: have you ever seen an estimate for how many fields are rented in the

248 UK? I would like to write something like: In the UK X% arable fields are rented, and our

249 finding suggests this has important implications for the level of *A. myosuroides* control

250 managers are incentivised to provide, and thus its spread [REF] and the evolution of

251 resistance [REF].]

252 We make three assumptions that impact how these results can be interpreted. Firstly,

253 the model was deterministic, so IPM strategies could not be risk averse to variability in

254 *A. myosuroides* populations and economics factors like crop prices.

255 Secondly, we assume that herbicide resistance was conferred by a target site mutations

256 that were already present in the population (although possibly at low frequencies). This is

257 why cycling was often favoured over stacking when two effective herbicides were available,

258 as cycling prolonged the useful life of both herbicides since the application of each was

259 spread out. There is growing evidence that non-target site resistance, which confers cross

260 resistance, is widespread [(Hicks *et al.*](#_bookmark29), [20](#_bookmark29)18). If generalized, non-target site, resistance

261 mechanisms are present, the total amount of herbicide exposure predicts resistance level

262 [(Hicks *et al.*](#_bookmark29), [2018),](#_bookmark29) and cycling will not help.

263 Finally we assume that herbicide is the only action that drives the evolution of resistance.

264 Any effective management tool will impose selection pressure, and so drive resistance to

265 that tool. In reality, the spring cropping and spot control sub-actions make heavy use

266 of glyphosate to control *A. myosuroides*. Glyphosate resistance has evolved on many

267 separate occasions in response to prolonged, heavy use [(Sammons & Gaines,](#_bookmark42) [2014).](#_bookmark42) As

268 glyphosate becomes a more important part of *A. myosuroides* management [(Hicks *et al.*](#_bookmark29),

269 [2018)](#_bookmark29) resistance is likely. [HELEN: anything missing from this para or the previous one?]

270 Our results show that farmers have an economic incentive to change their management in

271 response to changes in *A. myosuroides* populations, spatial variation in its effect on wheat

272 yields, and changes in commodity prices. [ALEXA: would be nice to conclude with a nice

273 summary statement on what a failure to be responsive will cost farmers, the economy as

274 whole and the environment, are at least as much as we can say at this point. Also be a

275 good place to flag your up coming work for any things that are still unresolved. If it is

276 all unresolved that is an important message as well I think.]

# 277 Supplementary material

278  **Appendix 1** Action Space

279  **Appendix 2** Population Model

280  **Appendix 3** Reward Function

281  **Appendix 4** Genetic Algorithm

|  |  |  |  |
| --- | --- | --- | --- |
| 282 | **Appendix 5** | Finding Which Initial Conditions and Model Parameters Lead to | Which |
| 283 | IPM Strategies |  |  |

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