Multi-Gene Insect Control Products & Refuge Issues
- is more always better?

Illinois Corn Breeders School

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Outline

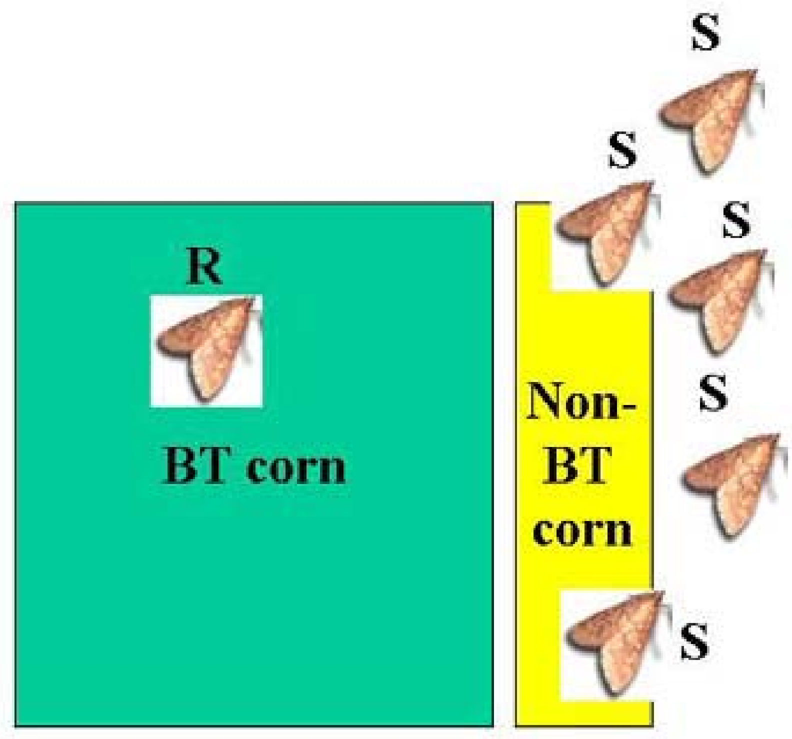
- **Bt traits & Insect Resistance Management (IRM)**
- **Optimum® AcreMax™ 1 products – a case study**
- **IRM – evolving with the technology**

IRM for Transgenic Insect Resistant Crops: A Brief History

- Regulated by U.S. EPA
- Framework developed more than a decade ago
- Initially harmonized across the industry
- Based on “High Dose – Refuge” assumptions
  - Cry1Ab and European corn borer
- Fifteen years later:
  - Much more data on many more pests
  - Many traits/pests may not fit “high dose” model
  - Initial “high dose” assumptions over-simplify adaptive responses in evolving populations (e.g. fitness costs & inbreeding depression, random mutations, etc.)
  - No longer harmonized across industry

High Dose - Refuge Strategy

- **High dose – kills >99%**
- **Low frequency of resistance genes**
- **Refuge produces susceptible insects to mate with rare resistant insects**
- **Essentially all SS and RS are killed**
- **Refuge placed to ensure random mating**



Optimum® AcreMax™ Insect Protection

Reduced & blended refuge

- Optimum® AcreMax™1 – rootworm refuge
- Optimum® AcreMax™2 – corn borer & rootworm refuge

Benefits:

- Trait durability
- Simplicity for growers
- Agronomically acceptable to growers
- Builds in refuge compliance
- Reduced pesticide use on refuge acres

Optimum® AcreMax™ 1 & 2 insect protection is not yet available for sale or use. Products will not be offered for sale or distribution until completion of field testing and approval by regulatory authorities.

Blended Refuge: Pros and Cons

Cons

- May be limited in size (%) due to unacceptable damage in high pest pressure regions
- May not be as durable as blocks/strips for single high dose toxins where older larvae may move readily between plants
- Requires more complex understanding of pest biology & field dose response

Pros

- Simple & efficient for growers
- Ensures refuge is planted
- Reduces insecticide use on refuge acres
- May be the most appropriate refuge for species with limited or no movement between adult emergence & mating
- Appropriate where high compliance rates are required to maintain durability

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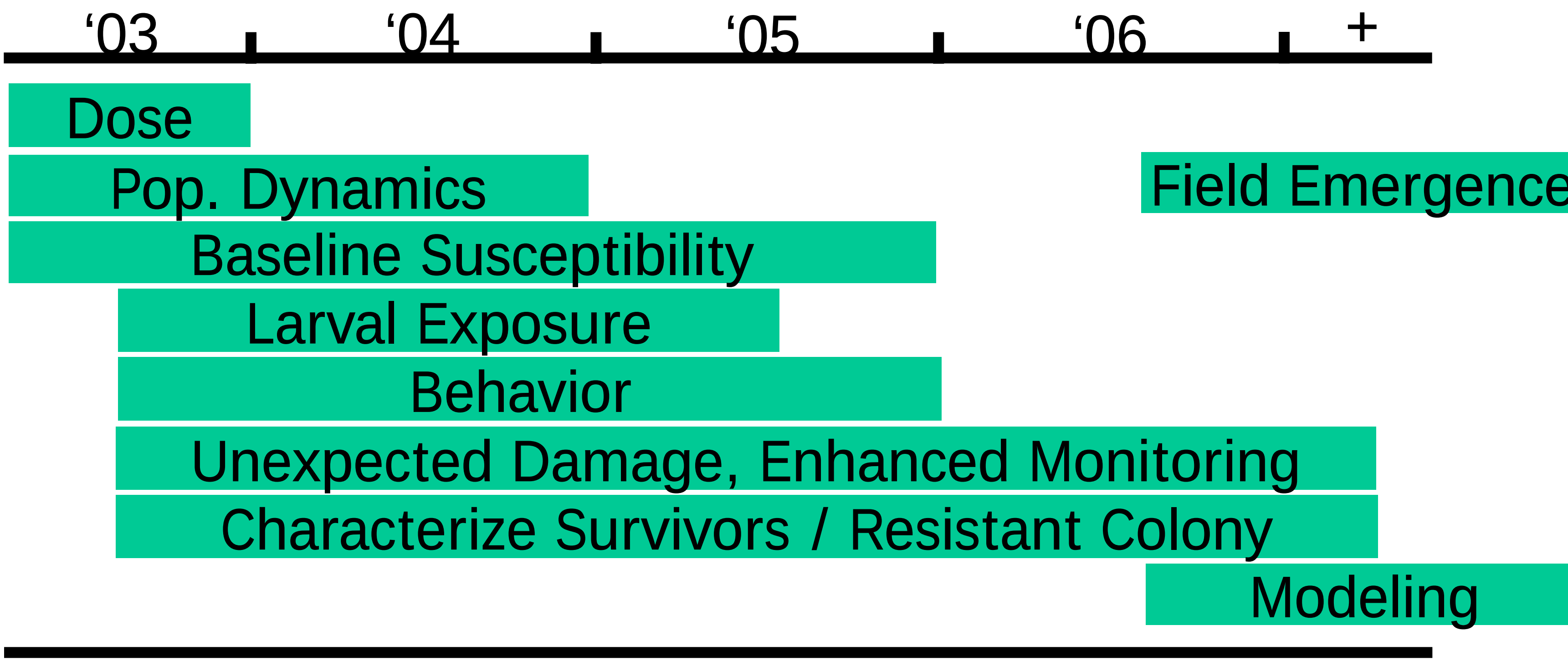
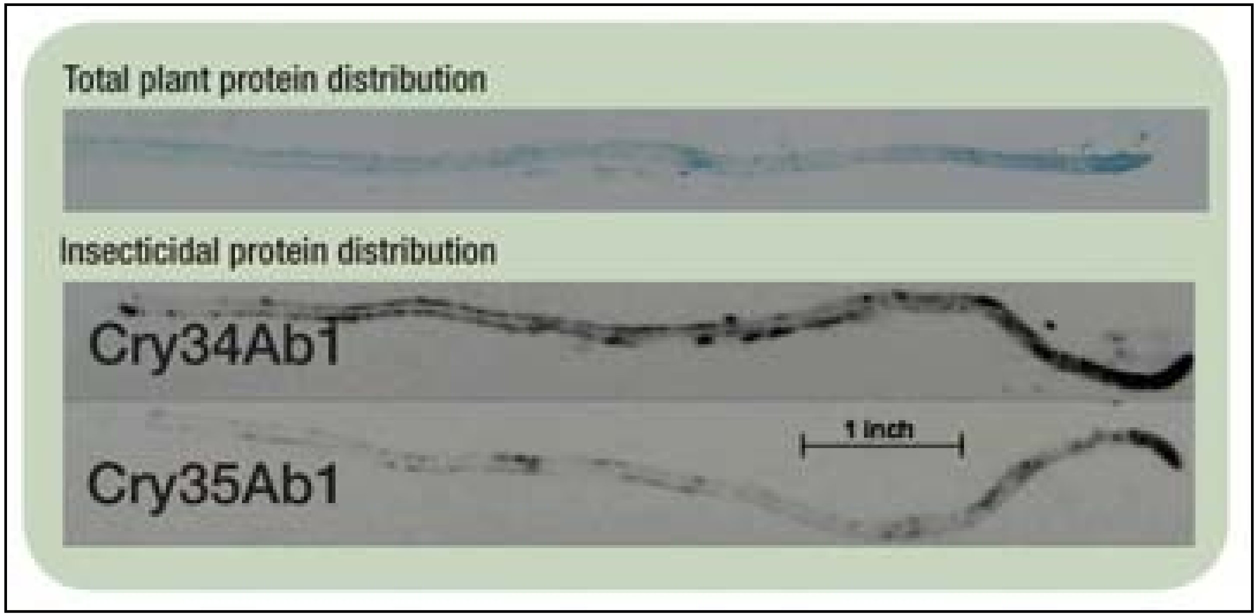
IRM Research Timeline

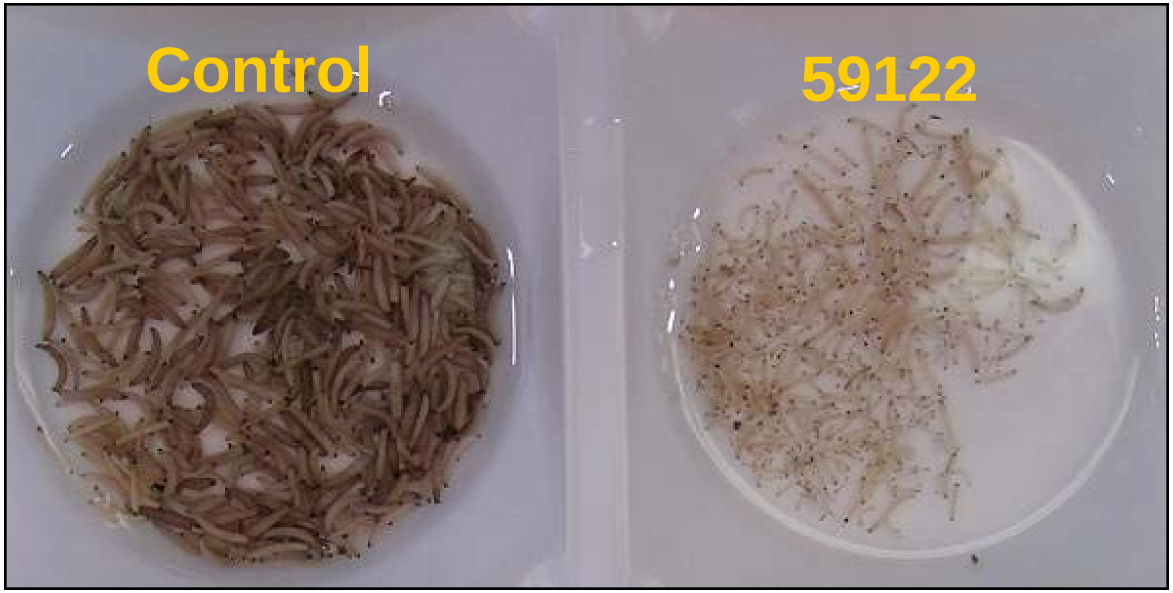


Larvae are Exposed to Variable Concentrations



- Spatial variation occurs within 59122 roots
- Provides effective exposure

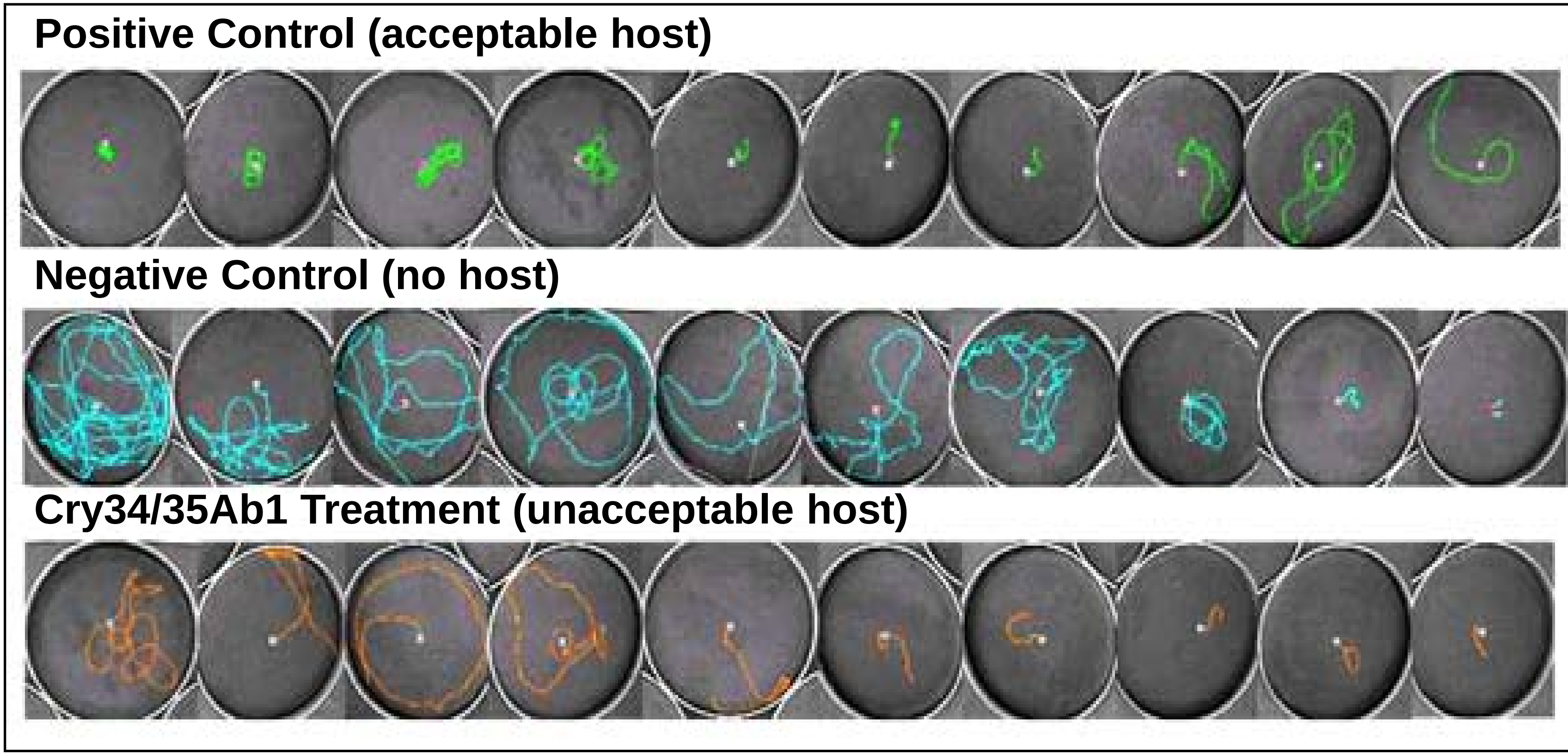
Effect is More Chronic Than Acute



Larvae Extracted After 17 Days of Exposure

Initial feeding <u>does not</u> result in direct mortality

Cry34/35Ab1 Makes 59122 a Less Acceptable Host



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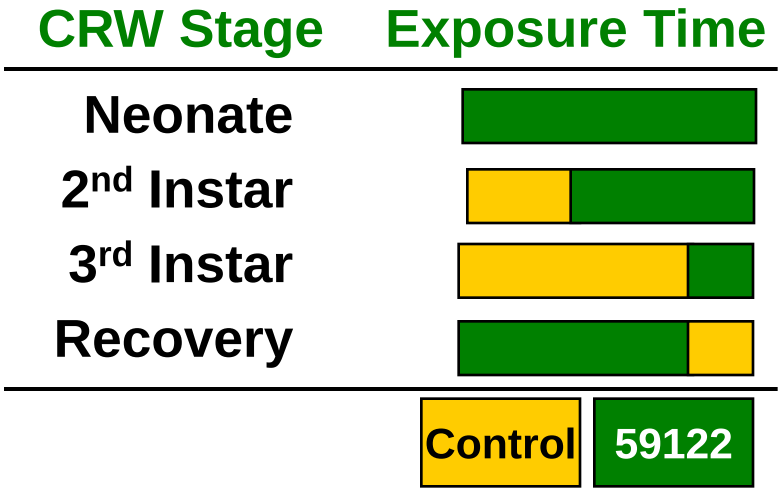
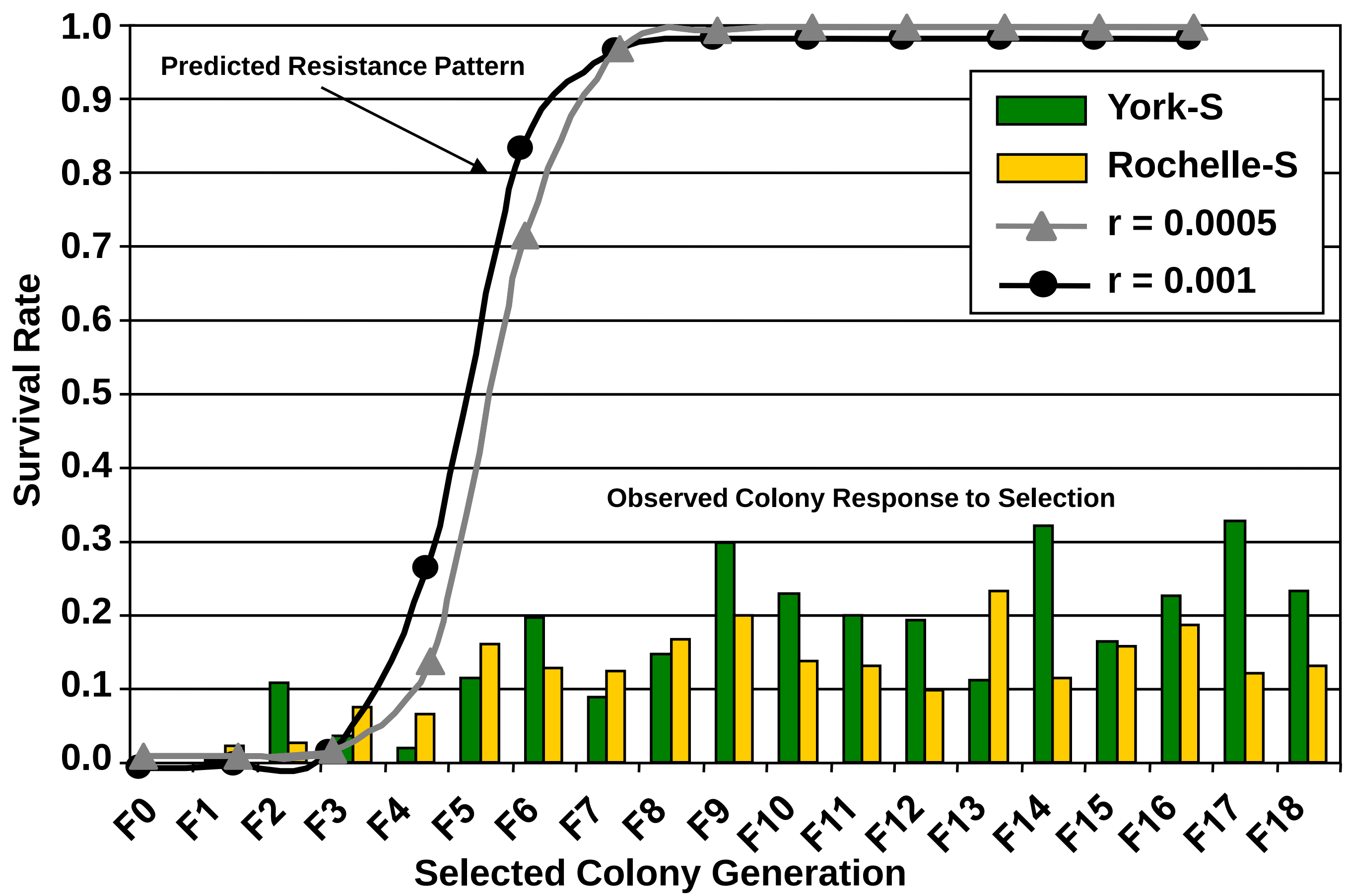
Exposed Larvae Can Recover



Adult Survival*	Average Weights
0.4%	-48%
26%	-50%
65%	-29%
114%	+2%

*all values relative to the appropriate control

Resistance to 59122 Does Not Appear to be Simply Inherited



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Life-History Traits of Beetles from Blends Similar to Refuge Beetles*

Female WCR Egg Production			
Treatment	Eggs / Female	Eggs / Female / Day	N
59122_P250	114 a	3.5 a	30
Seed Blend	268 bc	7.8 b	30
Control	261 ab	7.7 b	29
Control_P250	356 c	9.8 b	30
Fishers's Protected LSD Test, P<0.05			

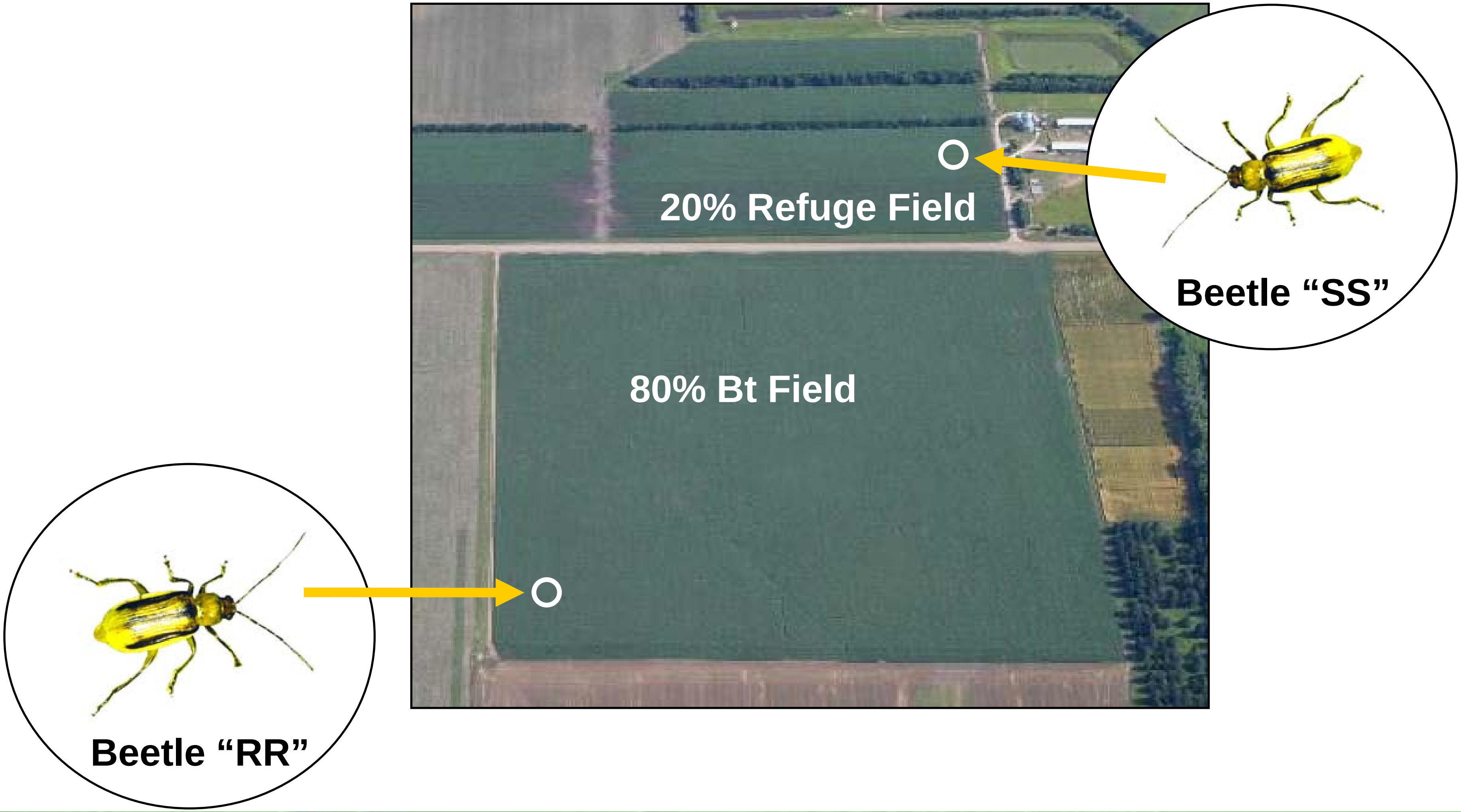
***Data generated by Meinke et al., University of Nebraska**

Simulation Models to Examine Trait Durability

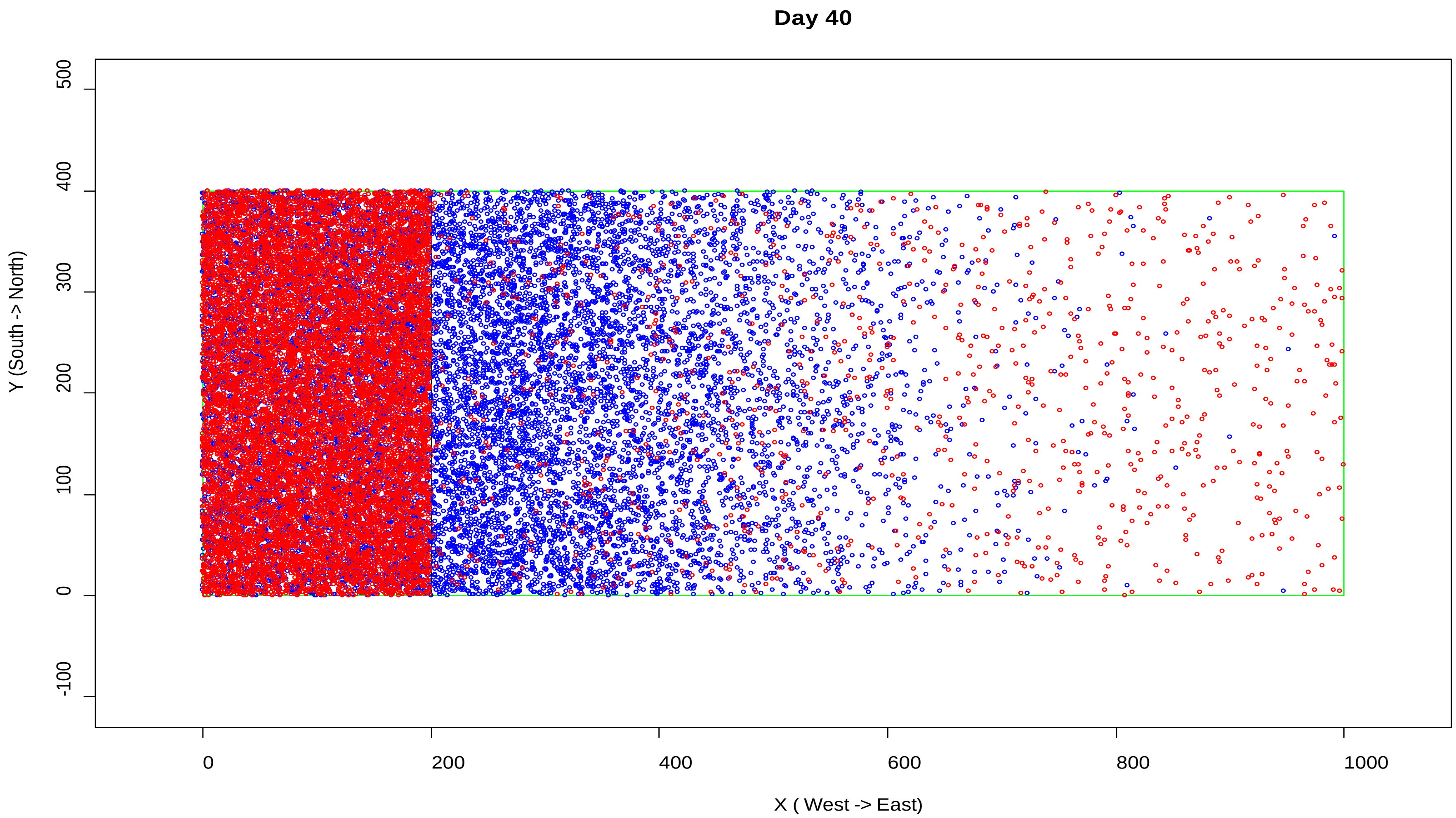
- **Tool for comparing IRM strategies**
- **Helps identify most important parameters**
- **Part of the 'weight of evidence' regulators use in assessing risk**

"…a good RM strategy should maintain population susceptibility to a transgenic insecticidal crop for longer than 10 years." (ILSI, 1999)

Adult Corn Rootworm Movement



Block Refuge Creates a Gradient for Male Dispersal- 20% Block (Red=Females Blue=Males)



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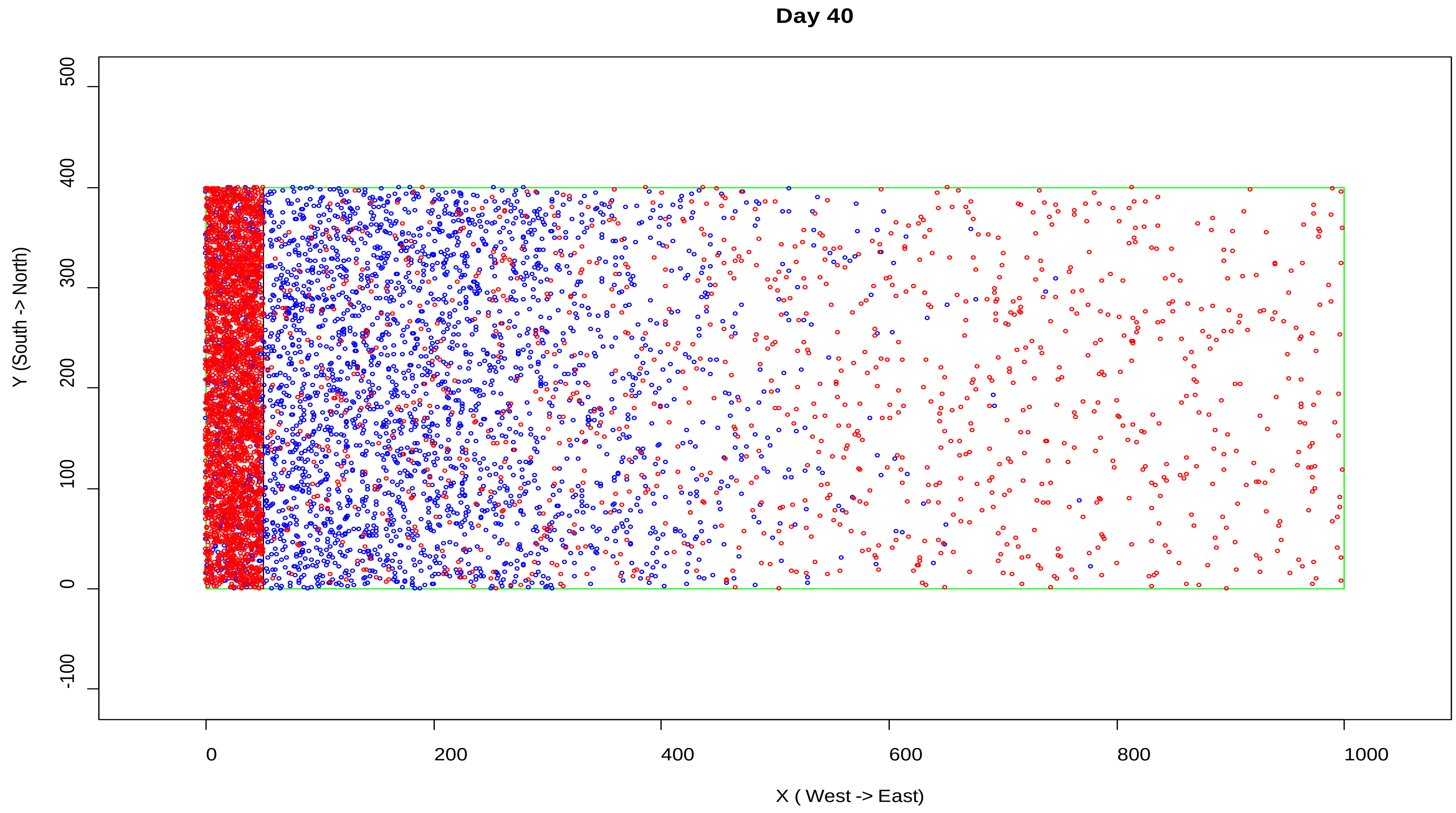
Block Refuge Creates a Gradient for Male Dispersal- 5% Block (Red=Females Blue=Males)



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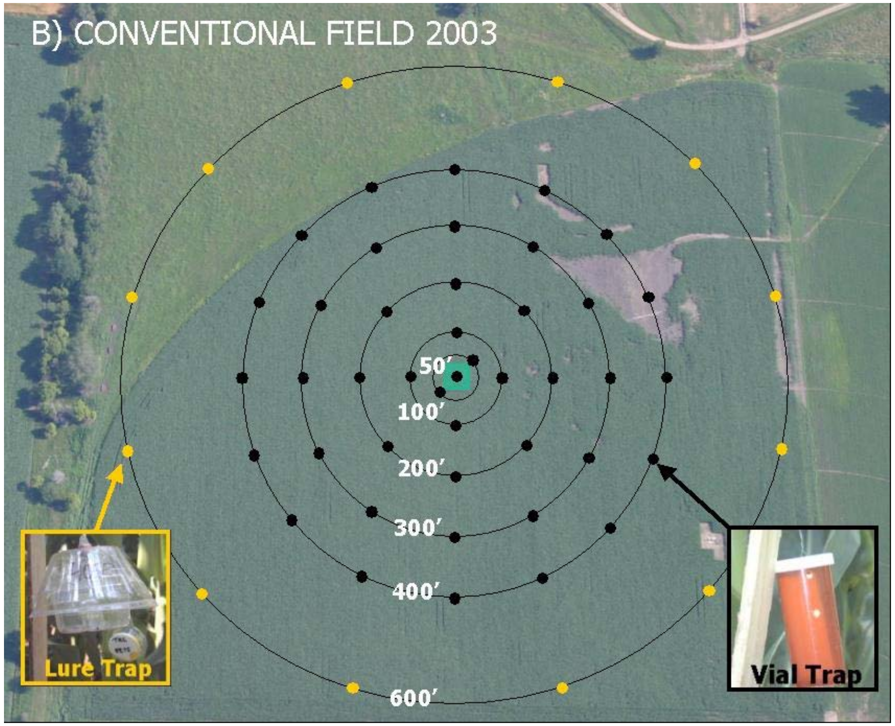
Parameters for Beetle Movement

WCR mark-recapture study

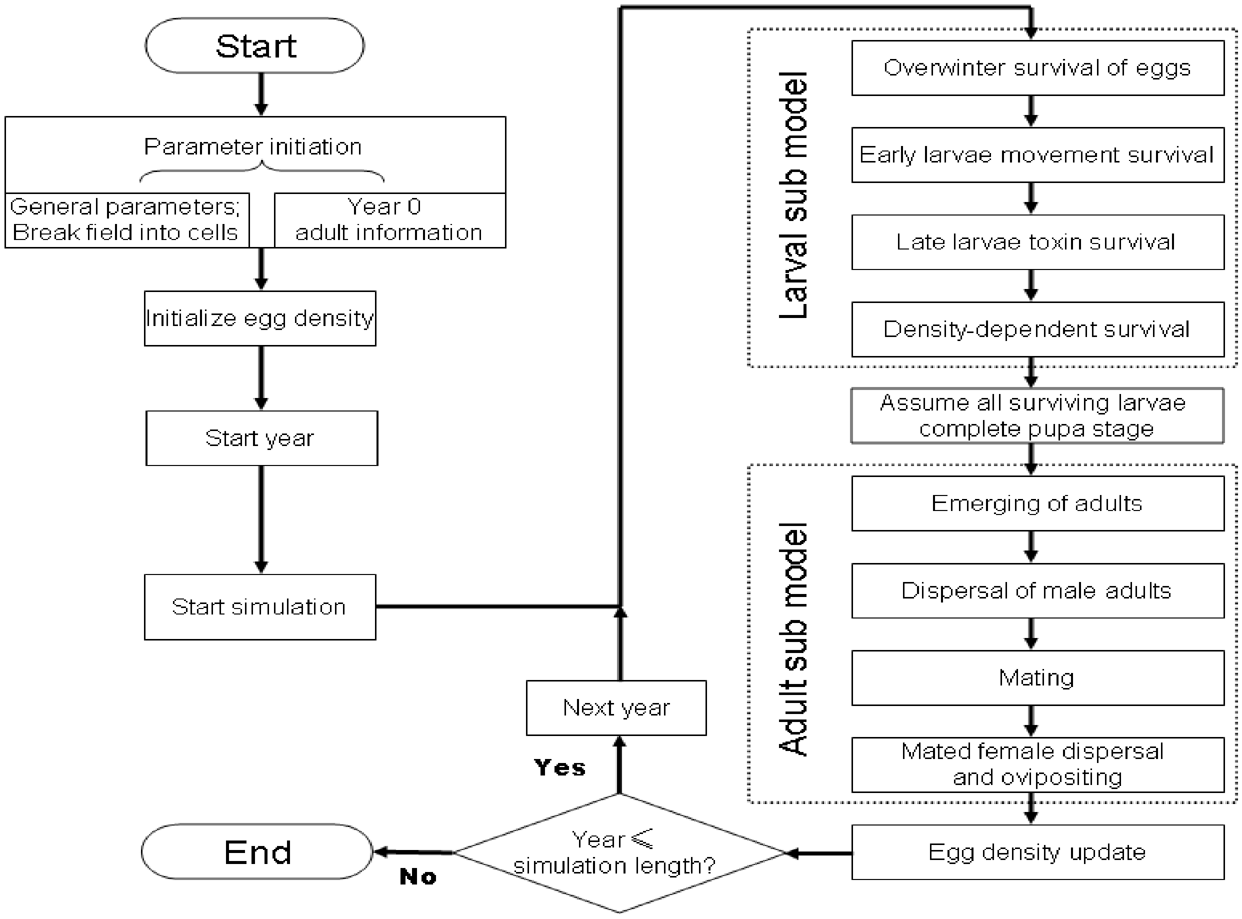
- Quantify how far WCR beetles move within the cornfield
- Determine where mating occurs relative to their emergence site
- Larvae marked through feeding on rubidium-treated corn plants
- Beetles captured in traps at fixed distances from the field center



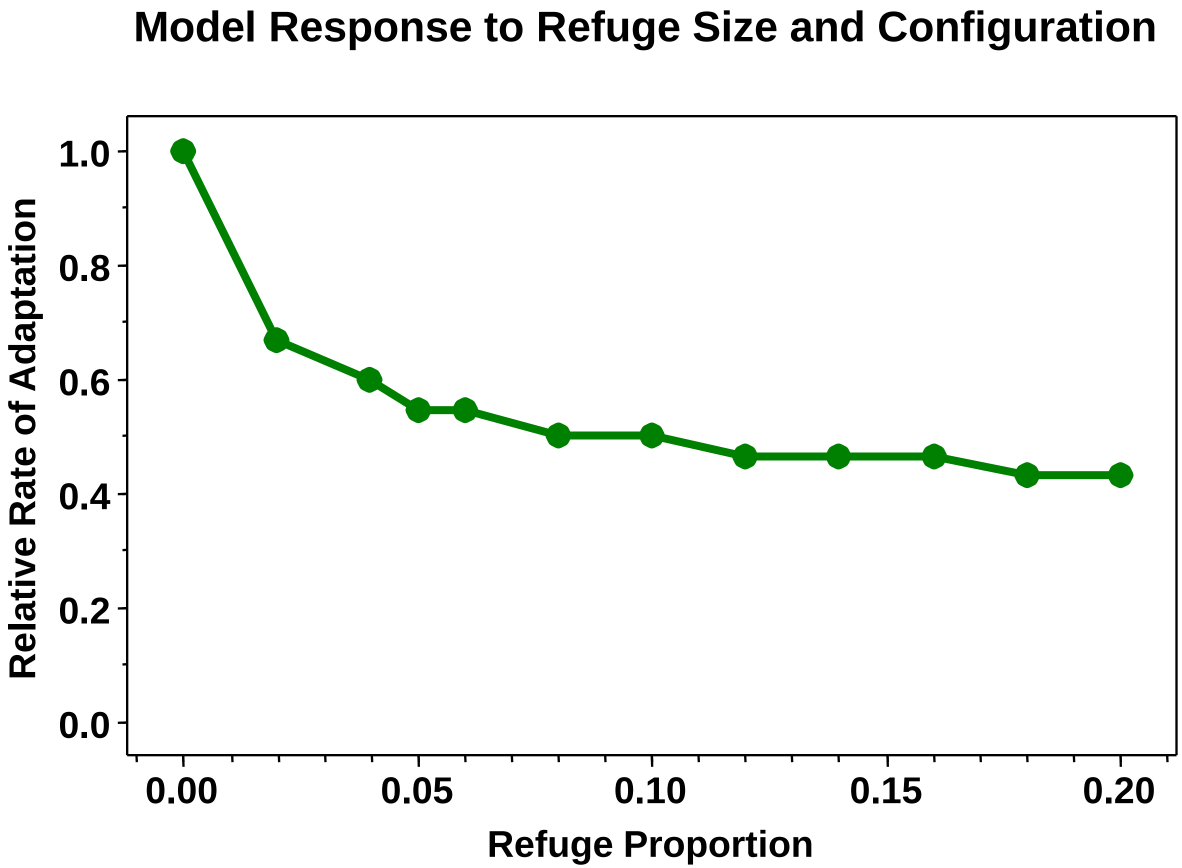
Modeling Approach: 59122 & Integrated Refuge

- Spatially explicit, landscape model
  - Includes beetle dispersal, probability of mating between refuge males and Bt females, and oviposition.
  - Supports up to a 2,500 hectare landscape (1 ha cells)
- Worst Case Assumptions:
  - simple recessive di-allelic resistance (not what we found in our selected colony)
  - continuous corn cropping system
  - 90% of females oviposit in their natal field

Modeling Durability



Sensitivity of Refuge Size with a Single Di-Allelic Recessive Locus



Prop. of Blended Refuge	RRA
0.05	0.55
0.1	0.46

Predicted Durability of Different Refuge Options

Refuge Deployment Strategy	Worst Case	Benchmark Parameters	Best Case
	Initial Resistance Allele Frequency=0.01 Dominance Value =0.1 surv-ss= 0.025 ovip-ss=0.32 ovip-rr =1	Initial Resistance Allele Frequency=0.001 Dominance Value =0.05 surv-ss= 0.0125 ovip-ss=0.32 ovip-rr =1	Initial Resistance Allele Frequency =0.0005 Dominance value=0.025, surv-ss= 0.0125 ovip-ss=0.32 ovip-rr =0.32
No refuge	3 years	5 years	9 years
20% block with variable locations and 70% compliance rate	4 years	8 years	13 years
5% blend	5 years	10 years	>20 years

Case Study Summary

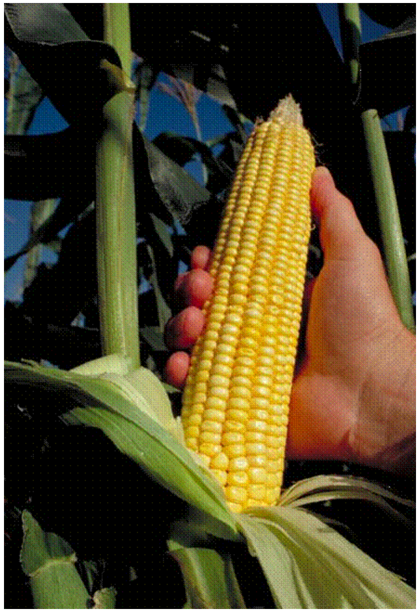
- 59122 is not high dose against CRW
- Characteristics of 59122 are compatible with integrated refuge
- Realistic data on CRW beetle movement have been incorporated into the model
- New modeling shows that a 5% blend is more durable than a 20% block
- OAM1 builds in grower compliance with CRW refuge requirements

Conclusions

- Insect control technologies are diversifying
- “one size fits all” IRM not appropriate
- Each trait x target needs individual consideration
- Growers need choices

Questions?

"…the latest knowledge is usually the best. Moreover, knowledge grows or dies. It cannot live in cold storage. It is perishable and must be constantly renewed."



~ Henry A. Wallace, co-founder of Pioneer Hi-Bred

Former U.S. Secretary of Agriculture & Commerce

Former Vice President of the United States