Mike Grimmer

BCPC Diseases Review, 19th October 2022
Erosion of varietal resistance in UK wheat

Key wheat varieties see slump in yellow rust rating

Farmers Weekly, 2019

Resistance breakdown: Septoria’s resurgence in 2021

Farmers Guide, 2021
Integration for **effective control**

How to combine:

- Mixtures: Fungicide + Fungicide
- Pyramiding: Host resistance + Host resistance
- Integration: Host resistance + Fungicide
Integration for **effective control**

Fungicide mode of action mixtures

**Multiplicative Survival Model (MSM):**

\[
\text{Fungicide A} + \text{Fungicide B} \\
90\% \text{ control} + 90\% \text{ control}
\]

\[
\text{Survival fraction} = 0.1 \times 0.1 = 0.01 \ (1\%)
\]

**Assumes independence of action**

Bliss, 1939. The toxicity of poisons applied jointly. *Annals of Applied Biology*
Integration for effective control

Pyramiding partial resistance loci

Grimmer, Boyd, Clarke, Paveley 2014 *Plant Pathology*

- AxE yellow rust
- AxB yellow rust
- AxC septoria
- AxS mildew
- AxS brown rust
- AxS yellow rust

Avocet x Saar Lillemo et al 2008
Avocet x Express Lin & Chen 2009
Alcedo x Brigadier Jagger et al 2011
Avalon x Cadenza data unpub.
Integration for effective control

Grimmer, Boyd, Clarke, Paveley 2014 *Plant Pathology*
Integration for long effective life

How to combine:

- Mixtures: Fungicide + Fungicide
- Pyramiding: Host resistance + Host resistance
- Integration: Host resistance + Fungicide
Integration for long effective life of fungicides

Van den Bosch et al. 2011 Plant Pathology 60, 597-606
Governing principle for pathogen evolution

\[ sT = (r_R - r_S) T \]

Selection
Rate of increase of resistant strain.
Rate of increase of sensitive strain.
Exposure time.

Milgroom & Fry, 1988 *Phytopathology*
van den Bosch et al. 2014 *Annual Review Phytopathology*
Governing principle for pathogen evolution

\[ sT = (r_R - r_S) T \]

Selection
Rate of increase of resistant strain.
Rate of increase of sensitive strain.
Exposure time.

**Strategy 1:** Reduce both \( r_R \) and \( r_S \)

**Strategy 2:** Reduce \( r_R \) relative to \( r_S \)

**Strategy 3:** Reduce exposure time
<table>
<thead>
<tr>
<th></th>
<th>Increase selection</th>
<th>No effect</th>
<th>Decrease selection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase dose</td>
<td>16</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Increase number of sprays</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Split the dose</td>
<td>10</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Add a mixture partner</td>
<td>1</td>
<td>6</td>
<td>46</td>
</tr>
</tbody>
</table>

Predictive value of Governing principle

van den Bosch, Oliver, van den Berg, Paveley 2014 *Annual Review Phytopathology*
Insensitive strain
Sensitive strain

Susceptible variety

Partially resistant variety

Pathogen density

Fraction resistant

Time
Selection for tebuconazole insensitive *Z. tritici*

Boxworth 2014, GS 70

% insensitive (without V136A)  

<table>
<thead>
<tr>
<th>Variety</th>
<th>No. applications</th>
<th>Total dose (units of tebuconazole)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susc</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Res</td>
<td>0</td>
<td>0.25</td>
</tr>
<tr>
<td>Res</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Res</td>
<td>2</td>
<td>0.75</td>
</tr>
<tr>
<td>Res</td>
<td>2</td>
<td>0.75</td>
</tr>
<tr>
<td>Int</td>
<td>2</td>
<td>0.75</td>
</tr>
<tr>
<td>Susc</td>
<td>2</td>
<td>1.0</td>
</tr>
<tr>
<td>Susc</td>
<td>2</td>
<td>1.5</td>
</tr>
<tr>
<td>Susc</td>
<td>3</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*F < 0.001, SED 8.7*

Genotyping data courtesy of Bart Fraaije
Virulent strain

Avirulent strain

Untreated

Fungicide treated

Pathogen density

Fraction virulent

Time
Governing principles predict:

- Partial (rate-limiting) host resistance reduces selection for fungicide insensitivity by:
  - Strategy 1 (reducing epidemic rates)
  - Strategy 2 (reducing dose)
  - Strategy 3 (reducing number of treatments/exposure)

- Qualitative host resistance reduces selection for insensitivity by:
  - Strategy 3 (reducing number of treatments/exposure)

- Fungicides reduce selection for virulence against partial and qualitative host resistance
The integration challenge:

Integration creates concurrent selection for virulence and insensitivity

How to:

- Use disease resistant varieties to minimise fungicide insensitivity evolution, whilst minimising virulence evolution
- Use fungicides to minimise virulence evolution, whilst minimising insensitivity evolution
Extending the durability of cultivar resistance by limiting epidemic growth rates

Kevin Carolan¹, Joe Helps², Femke van den Berg¹,², Ruairidh Bain³, Neil Paveley⁴ and Frank van den Bosch¹

¹ Rothamsted Research, Harpenden AL5 9SL, UK
² FERA, York Y041 1LZ, UK
³ SRUC, Edinburgh EH9 3JG, UK
⁴ ADAS, High Mowthorpe, Malton, North Yorkshire Y017 8BP, UK

Cultivar resistance is an essential part of disease control programmes in many agricultural systems. The use of resistant cultivars applies a selection pressure on pathogen populations for the evolution of virulence, resulting in loss of disease control. Various techniques for the deployment of host resistance genes have been proposed to reduce the selection for virulence, but these are often difficult to apply in practice. We present a general technique to maintain the effectiveness of cultivar resistance. Derived from classical population genetics theory, any factor that reduces the population growth rates of both the virulent and avirulent strains will reduce selection. We model the specific example of fungicide application to reduce the growth rates of virulent and avirulent strains of a pathogen, demonstrating that appropriate use of fungicides reduces selection for virulence, prolonging cultivar resistance. This specific example of chemical control illustrates a general principle for the development...
Weak host resistance

Strong host resistance

1 QTL

3 QTL

T95, years

Dose
Years of effective control:
- Zero
- Low
- High
AHDB Wheat Growth Guide
Generic:
Any independent disease control method that reduces the epidemic growth rate will reduce selection

Specific:
• Resistant cultivars reduce selection for fungicide insensitive pathogen strains.
• Fungicides reduce selection for virulent pathogen strains.
• More sustainable to integrate and balance chemical and genetic crop protection, than to be heavily dependent on either genetics or chemistry
Summary

- Cereal farmers need effective and durable control of multiple diseases
- Effectiveness of integrating control predictable
- But control drives pathogen evolution
- Evolution according to simple governing principle
- Good experimental evidence on insensitivity evolution
- Good tools for virulence evolution experiments
Future perspectives

- Experimental evidence needed for virulence evolution with fungicide use
- Evolutionary potential of different types of resistance gene
- Role of sexual / asexual reproduction on pathogen evolution
- Role of fitness penalties in slowing fungicide resistance
- Impact of Integrated Pest Management (IPM) approaches
- Breeding for alternative traits not affected by evolution
  - Disease escape – traits that reduce contact between inoculum and susceptible tissues
  - Disease tolerance – traits that reduce the impact of disease on yield
Thank you!
Predictive power of LPs / year on sqrt FDR time (n = 59, P = <0.001).

\[ R^2 = 0.42 \]

Grimmer et al. (2014)  
Pest Manag Sci
Frequency distribution: First Detection of Resistance time (n = 61)
<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Fungicide</th>
<th>Agronomic system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kingdom</td>
<td>FRAC MOA</td>
<td>Crop species</td>
</tr>
<tr>
<td>Phylum</td>
<td>FRAC group</td>
<td>Country</td>
</tr>
<tr>
<td>Class</td>
<td>Chemical group</td>
<td>Area treated – foliar</td>
</tr>
<tr>
<td>Suborder</td>
<td>Fungicide active substance</td>
<td>Area treated – seed</td>
</tr>
<tr>
<td>Family</td>
<td>Target protein length</td>
<td>Area treated – total</td>
</tr>
<tr>
<td>Genus</td>
<td>Target gene copy number</td>
<td>Use intensity (trt. ha/crop ha)</td>
</tr>
<tr>
<td>Species</td>
<td>Molecular weight</td>
<td>Cropped area</td>
</tr>
<tr>
<td>Trophic type</td>
<td>Solubility ratio</td>
<td>Country area</td>
</tr>
<tr>
<td>Mono/poly cyclic</td>
<td>H-bond donor/acceptor potential</td>
<td>Agronomic intensity</td>
</tr>
<tr>
<td>Resting stage</td>
<td>Topological polar surface area</td>
<td>Outdoor/protected</td>
</tr>
<tr>
<td>Resting structure</td>
<td>Complexity</td>
<td>Annual/perennial</td>
</tr>
<tr>
<td>Asexual/sexual</td>
<td>Action</td>
<td></td>
</tr>
<tr>
<td>Asexual spore type</td>
<td>Systemicity</td>
<td></td>
</tr>
<tr>
<td>Asexual spore volume</td>
<td>Application method</td>
<td></td>
</tr>
<tr>
<td>Sexual spore type</td>
<td>Used in mixtures</td>
<td></td>
</tr>
<tr>
<td>Sexual spore volume</td>
<td>Efficacy at introduction</td>
<td></td>
</tr>
<tr>
<td>Vegetative ploidy level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. host species/genera</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apparent epidemic growth rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basic reproductive number (R0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latent period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Latent periods per year</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Trait-based risk assessment model

\[ \text{Sqrt (FDR)} = \text{Constant} + \]
\[ \quad \text{Latent periods per year (number)} \]
\[ \quad \text{Fungicide complexity (PubChem rating)} \]
\[ \quad \text{Number of crop host species (1-9 or 10+)} \]
\[ \quad \text{Agronomic system (protected or outdoor)} \]

No significant interactions

F probability < 0.001

\[ \text{Sqrt (FDR)} = \text{Constant} - 0.027 \times \text{LP/year} - 0.0024 \times \text{Fung complexity} \]
Phases of fungicide resistance evolution

Emergence

Introduction of fungicide

Time

Effective life

Sensitive population

Loss of effective control

Selection

Phases of fungicide resistance evolution