Assessing disease resistance in chickpeas through the bivariate analysis of Gaussian and binomial traits.

Aidan McGarty[1]
Brian Cullis[1], Ahsan Asif[2] and Kristy Hobson[2]

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Mixed Models and Experiment Design Lab (MMaEDL)[1]
National Institute for Applied Statistics Research Australia
University of Wollongong
`amcgarty@uow.edu.au`

Chickpea Breeding Australia[2]
NSW Department of Primary Industries | Agriculture

Overview

- **Motivation**
  - Context
  - Complexities
- **The statistics of the problem**
  - Choice of model
- **Results**
  - Parametric bootstrapping

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- These factors lead to a complex statistical analysis

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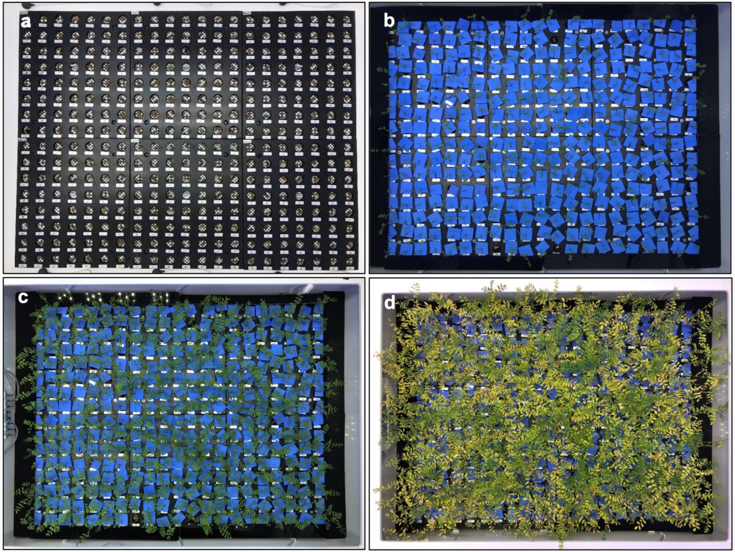
- Hydroponics experiments provide high throughput low cost alternatives to field experiments

Scenario - Hydroponic



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Tank	Rack	HRange	HRow	Variety	TotalLeaf	DisLeaf
1	1	1	1	A	6	2
1	1	2	1	B	5	3
1	1	3	1	C		
1	1	4	1	D	11	6
1	1	5	1	F	13	9
1	1	6	1	A	15	7

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FCol	FRow	Variety	Risk1	Dead1	Risk2	Dead2	Risk3	Dead3	ExpectedLife
1	1	A	16	0	16	12	4	15	1.57
1	2	B	16	0	16	0	16	0	9.39
1	3	C	16	0	16	0	16	2	4.01
1	4	D	10	0	10	7	3	9	1.75
1	5	E	19	0	19	2	17	7	2.98
1	6	A	16	0	16	4	12	7	2.87

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- We choose a bivariate generalised linear mixed model (GLMM) using ASReml-R

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- To overcome this the two data frames are merged by variety in a non-unique way

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WPlot	Variety	FCol	FRow	Tank	Rack	HRange	HRow	DL*	TL*	EL*
1	A	1	1	1	1	1	1	2	6	1.57
2	B	1	2	1	1	2	1	3	5	9.39
3	C	1	3	1	1	3	1			4.01
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*DL = Number of chlorotic leaves (hydroponic), *TL = Number of total leaves (hydroponic) and *EL = Expected lifetime (field)

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- WPlot arbitrarily joins field and hydroponic observations by common varieties, however as evident in WPlot 5 and 6 not all field and hydroponic observations can be matched

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- We would also like to include random effects $\mathbf{u} = (\mathbf{u}_g^\intercal, \mathbf{u}_{p_H}^\intercal, \mathbf{u}_{p_F}^\intercal)^\intercal$ which are either shared genetic effects $\mathbf{u}_g$ or non-shared peripheral effects $\mathbf{u}_{p_H}$ and $\mathbf{u}_{p_F}$, for the hydroponic and field experiments respectively

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- We can then write the distributions $\mathbf{y}_H|\mathbf{u}$ and $\mathbf{y}_F|\mathbf{u}$ conditional on the random effects $\mathbf{u}$ with associated probability density functions (PDF) $f_{Y_H|U}$ and $f_{Y_F|U}$

Model - Hydroponic Conditional Distribution

$$E(y_{H_i}|\mathbf{u}) = \mu_{H_i}$$

$$g(\mu_{H_i}) = \eta_{H_i} = \mathbf{x}_{H_i}^\top \boldsymbol{\tau} + \mathbf{z}_{H_i}^\top \mathbf{u}$$

$$V(y_{H_i}|\mathbf{u}) = \phi_H \mu_{H_i}(1 - \frac{\mu_{H_i}}{n_{TL_i}})$$

- for $i = 1, \ldots, n_H$ where $g()$ is the logit link function
- $\mathbf{x}_{H_i}$ and $\mathbf{z}_{H_i}$ are indicator/covariate vectors of length c_X and c_Z relating to the fixed ($\boldsymbol{\tau}$) and random ($\mathbf{u}$) effects for the ith observation in the hydroponic experiment
- ϕ_H represents the dispersion parameter and n_{TL_i} are the binomial totals for the ith observation in the hydroponic experiment

Model - Field Conditional Distribution

$$E(y_{F_i}|\mathbf{u}) = \eta_{F_i} = \mathbf{x}_{F_i}^{\top}\boldsymbol{\tau} + \mathbf{z}_{F_i}^{\top}\mathbf{u}$$

$$V(y_{F_i}|\mathbf{u}) = \sigma_F^2$$

- for $i = 1, \ldots, n_F$
- $\mathbf{x}_{F_i}$ and $\mathbf{z}_{F_i}$ are indicator/covariate vectors of length c_X and c_Z relating to the fixed ($\boldsymbol{\tau}$) and random ($\mathbf{u}$) effects for the ith observation in the field experiment
- σ_F^2 is the field residual variance

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- For convenience we allow $\boldsymbol{\kappa}$ to contain all parameters in $\mathbf{G}_g$, $\mathbf{G}_{p_H}$ and $\mathbf{G}_{p_F}$ along with ϕ_H and σ_F^2

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- The first term of which is not analytically tractable and hence requires an alternative to classical likelihood inference - therefore PQL is used to approximate the likelihood (Collins, 2008)

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- In the case of the non-genetic effects, we specify $\mathbf{G}_{p_H}$ and $\mathbf{G}_{p_F}$ as block diagonal matrices

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- This parameterisation is known as "reduced rank + diag" and is convenient as estimates of the λ_{i_j}, $i = a, e$, $j = H, F$ cannot go outside the parameter space unlike the "σ" parameters in the unstructured parameterisation

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- Due to the non-Gaussian nature of the response recorded in the hydroponic experiment we use PQL, an approximate likelihood method as the likelihood analytically intractable
- For the genetic effects, which are our main interest, we specify a variance structure which allows for covariance between experiments

Model - ASReml

```r
asreml(fixed = cbind(DL,EL) ~ trait + trait:VarietyDrop,
       random =~ rr(trait):vm(Variety, K) + at(trait,"EL"):vm(Variety, K) +
         rr(trait):ide(Variety) + at(trait,"EL"):ide(Variety) +
         at(trait, "DL"):Tank + at(trait, "DL"):Tank:Rack +
         at(trait, "DL"):Tank:Rack:HRow + at(trait, "DL"):Tank:Rack:HRange +
         at(trait, "EL"):FRow + at(trait, "EL"):FCol,
       residual = ~id(WPlot):diag(trait),
       data = df,
       family = list(asr_binomial(total = "TL"), asr_gaussian()),
       na.action = na.method(x="include",y="include"))
```

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- The researcher would also like a confidence interval on this estimate
- To do so while also assessing potential bias in the PQL estimates, a known issue impacting parameter estimation (Breslow & Lin, 1995) we implement parametric bootstrapping

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- $i = 1, \ldots, p$ where p is the number of parameters, $\hat{\theta}_i^{(j)}$ is the estimate of the ith parameter at the jth iteration with t being the final iteration

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- A total of 2000 bootstrap simulations were generated, of these 726 were omitted due to non-convergence
- This was based on a criteria for parameter convergence;

$$\Delta_{\text{norm}} = \sqrt{\frac{\Sigma_i(\hat{\theta}_i^{(t)} - \hat{\theta}_i^{(t-1)})^2}{\Sigma_i \hat{\theta}_i^{(t)2}}}$$

- $i = 1, \ldots, p$ where p is the number of parameters, $\hat{\theta}_i^{(j)}$ is the estimate of the ith parameter at the jth iteration with t being the final iteration
- After 50 iterations simulations where $\Delta_{\text{norm}} > 0.001$ were excluded

Parametric Bootstrapping - Applied

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- The remaining 1274 simulations resulting in an average total genetic correlation of -0.54 with an associated 95% confidence interval (-0.70,-0.36)

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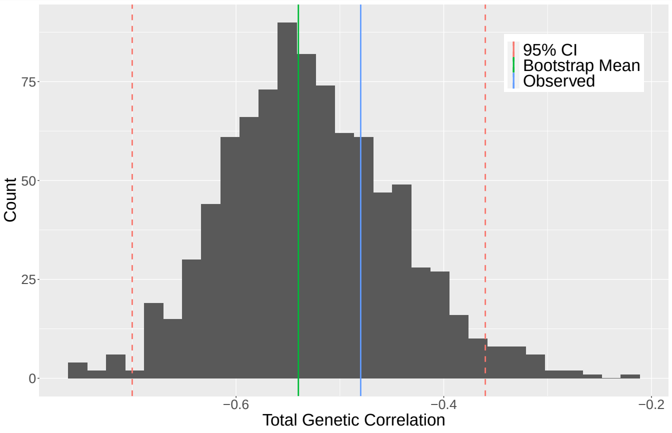

Parametric Bootstrapping - Sampling Distribution

Parameter	Obs	BootMean
σ^2_{Tank}	0.082	0.077
σ^2_{Rack}	0.022	0.022
σ^2_{FRow}	0.000	0.014
σ^2_{FCol}	0.013	0.025
σ^2_{HRange}	0.038	0.035
σ^2_{HRow}	0.092	0.088
ψ_{a_F}	0.000	0.023
ψ_{e_F}	2.458	1.617
λ_{a_H}	0.151	0.335
λ_{a_F}	-1.074	-0.032
λ_{e_H}	0.376	0.997
λ_{e_F}	-0.591	-0.874
ϕ_H	1.095	0.965
σ^2_F	3.593	3.571

σ^2_j, $j =$ Tank, Rack, FRow, FCol, HRange and HRow are the variance components associated with the peripheral random effects, ψ_{a_F}, ψ_{e_F}, λ_{a_H}, λ_{a_F}, λ_{e_H} and λ_{e_F} are the genetic parameters and ϕ_H and σ^2_F are the hydroponic dispersion and field residual variance parameter respectively

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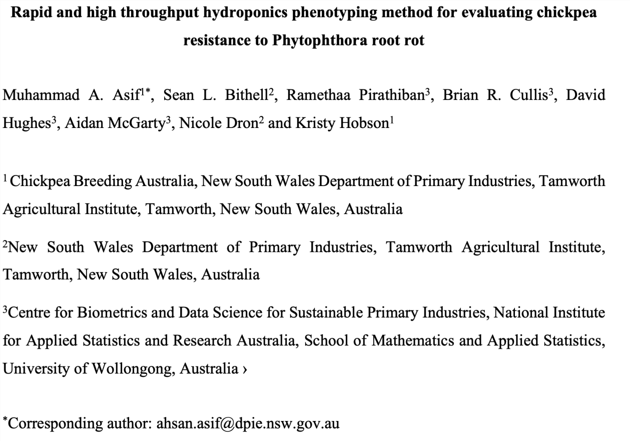
- The resulting analysis gave a quantification of the level of agreement between PRR resistance for the two experiments
- Parametric bootstrapping provided assessment of parameter estimation bias and indicated the associated 95% bootstrap CI for the total genetic correlation does not contain 0

Paper



Rapid and high throughput hydroponics phenotyping method for evaluating chickpea resistance to Phytophthora root rot

Muhammad A. Asif[1*], Sean L. Bithell[2], Ramethaa Pirathiban[3], Brian R. Cullis[3], David Hughes[3], Aidan McGarty[3], Nicole Dron[2] and Kristy Hobson[1]

[1] Chickpea Breeding Australia, New South Wales Department of Primary Industries, Tamworth Agricultural Institute, Tamworth, New South Wales, Australia

[2] New South Wales Department of Primary Industries, Tamworth Agricultural Institute, Tamworth, New South Wales, Australia

[3] Centre for Biometrics and Data Science for Sustainable Primary Industries, National Institute for Applied Statistics and Research Australia, School of Mathematics and Applied Statistics, University of Wollongong, Australia ›

[*] Corresponding author: ahsan.asif@dpie.nsw.gov.au

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