WHAT IF ALL VARIANTS ARE RARE?

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ROTHAMSTED RESEARCH

INTRODUCTION

Figure 1. Wheat TILLING panel in the robotic Field Scanalyzer (Virlet *et al.* 2017).

(Uauy 2017)

- TILLING (Targeting Induced Local Lesions In Genomes) is a method used to create a **mutagenised** population allowing the identification of point mutations within genes of interest (Krasileva *et al.* 2017).
- The relative contribution of **(ultra) rare variants** to quantitative genetic variation is largely unclear, despite recent advances in genomics. One reason for this is that natural populations tend to violate the assumptions of **genome-wide association** and **genomic heritability** models.
- Field-based phenotyping tools have been used to identify genes/QTL throughout the crop growth cycle for **dynamic phenotypes** (Lyra *et al.* 2020).

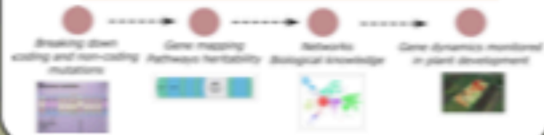
MAIN OBJECTIVES

The goals of this study were to:

(i) perform gene-based association analysis using collapsing models into non-synonymous, synonymous, and non-coding mutations sets,

(ii) partition the variance of (a) mutation types over the course of the growing season, (b) single genes, and (c) chromosomes.

QUANTITATIVE GENETICS PIPELINE



MATERIALS AND METHODS

- We performed quantitative genomic analyses (see pipeline) in an experimental TILLING population of hexaploid wheat cv. Cadenza (**~1145 lines**) in which all chemically induced mutations were either rare or unique, starting with a (mostly) uniform genomic background,
- The field trials were conducted in John Innes Centre (JIC) and at the **Field Scanalyzer** phenotyping platform at Rothamsted Research, Harpenden, UK,
- Using exome re-sequencing data, we partitioned the complete set of **~7M mutations** (**~77K genes**) into non-synonymous, synonymous, and non-coding sets,
- We conducted **gene-based analysis** (collapsing models) and variance component analyses for **three phenotypic traits** (i.e. plant height, heading/flowering time, and senescence).

ULTRA-RARE VARIANTS IN THE WHEAT TILLING POPULATION

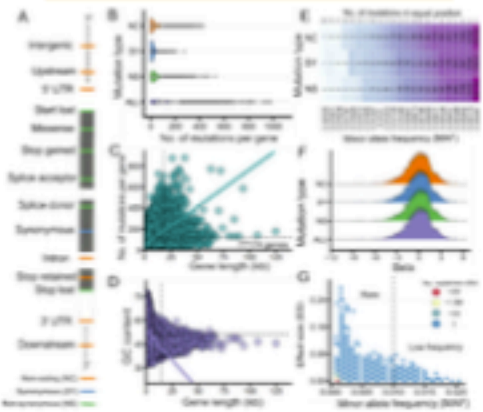


Figure 2. Mutation variants summary in the wheat TILLING population.

GENE SCANNING AND VARIANCE PARTITIONING

- Gene scanning of variants revealed **association signals** coming mostly from **non-synonymous** and **synonymous substitutions** for plant height (Fig. 3),
- Breaking down the genetic variance of **chromosomes** and **single genes** revealed insights of the contribution of **ultra-rare variants** to phenotypic traits (Fig. 3).

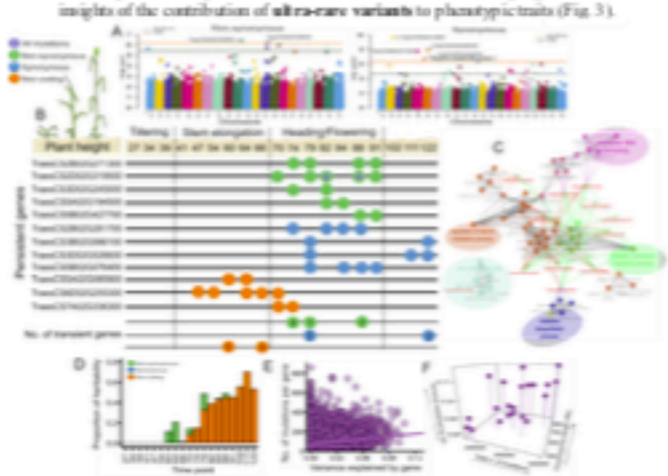


Figure 3. Summary of the quantitative genetic analysis of plant height in the wheat TILLING population.

CONCLUSION

This approach will lead to the **identification of candidate genes** across a range of phenotypic traits and contribute to the development of novel analytical methodology, ultimately enhancing our understanding of the **importance of (ultra) rare variants** in both natural and experimental populations.

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