

MiReN: AN OPTIMIZATION TOOL FOR DATA-DRIVEN DISCOVERY OF GLOBAL REGULATORY PHENOMENA DURING HEAT STRESS IN RICE



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1. Highlights

- Abiotic stresses during early seed development adversely affect the seed size and quality at maturity.
- □ To understand heat stress response in rice, a **temporal transcriptomic** analysis was performed.
- A mathematical optimization framework, MiReN, was developed to identify the minimal regulatory relationships in rice seed.
- □ A new, comprehensive, genome-scale metabolic model of rice seed is under development, enhanced by MiReN.
- □ A multi-tissue plant-scale model will allow us to answer important

4. Minimal Regulatory Network (MiReN) Identifier

- Gene regulatory relationships are **hierarchical** and **not always linear**.
- MiReN finds the **minimal number of regulatory influence** on a gene that agrees with transcriptomic data.
- The **interaction coefficient** defines the extent of activation or inhibition of a gene by a regulator.

Challenges



minimize	regulatory connections [M	iReN]
subject to,		
<i>minimize</i> subject to,	discrepancy with experimental gene expression data	
Change Bounds	e in gene expression = \sum f(Interaction coeff. × expr of regulators) s on interaction coefficient	for every gene

biological questions regarding stress response and will accelerate the development of stress-tolerant crop cultivars.

Variable Bounds

Total number of regulatory interactions < cutoff



6755 stress-responsive genes

References

39 Cellular Processes GO terms identified

5. Identified Regulatory Relationships

- SLR1 represses GA response pathway.
- Disease resistance gene XA21 controls several transcriptional repressors related to stress tolerance.
- Underlying circadian regulation?



- **Predicted** regulatory influence for 228 stress responsive rice Transcription factors
- Most **prominent** heat stress-responsive transcription factors: Elongation factors
 - Ethylene Response factors MYB



(Jan and Komatsu 2006)

Seo et al 2011;

Sharma et al 2013

3. Differential Gene Expression: Clustering



6. Future Directions

Genome-scale **metabolic** model of rice seed is coming soon, integrated with regulatory information from MiReN.

bZIP

MADS-M

- Tissue-specific models of plant root, seed, leaf, and stalk will be assembled into a plant-scale metabolic model.
- Knowledge gained from transcriptomic analyses and regulatory relationships will guide the development of stress-tolerant crop varieties.
- Artificial Intelligence for making decisions on robust engineering targets for crop stress-tolerance and yield from vast omics' databases is needed.

Stalk-

1. Jan, A. and S. Komatsu (2006). "Functional Characterization of Gibberellin-Regulated Genes in Rice Using Microarray System." Genomics, Proteomics & Bioinformatics 4(3): 137-144.

2. Seo, Y. S., et al. (2011). "Towards establishment of a rice stress response interactome." PLoS Genet 7(4): e1002020.

3. Sharma, R., et al. (2013). "Recent advances in dissecting stress-regulatory crosstalk in rice." Mol Plant 6(2): 250-260.

4. Henry, C. S., et al. (2010). "High-throughput generation, optimization and analysis of genome-scale metabolic models." Nat Biotechnol



5. Lakshmanan, M., et al. (2015). "Unraveling the Light-Specific Metabolic and Regulatory Signatures of Rice through Combined in Silico Modeling and Multiomics Analysis." Plant Physiol 169(4): 3002-3020. 6. Grafahrend-Belau, E., et al. (2009). "Flux balance analysis of barley seeds: a computational approach to study systemic properties of

central metabolism." Plant Physiol 149(1): 585-598.