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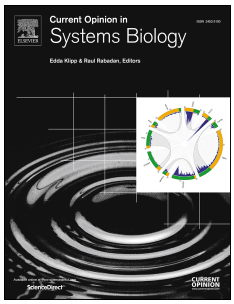

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PII: S2452-3100(17)30076-8

DOI: 10.1016/j.coisb.2017.04.002

Reference: COISB 44

To appear in: *Current Opinion in Systems Biology*

Received Date: 16 November 2016

Revised Date: 29 March 2017

Accepted Date: 7 April 2017

Please cite this article as: Bussemaker HJ, Causton HC, Fazlollahi M, Lee E, Muroff I, Network-based approaches that exploit inferred transcription factor activity to analyze the impact of genetic variation on gene expression, *Current Opinion in Systems Biology* (2017), doi: 10.1016/j.coisb.2017.04.002.

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ACCEPTED MANUSCRIPT

[Manuscript, Curr. Op. Syst. Biol., Review, ~2000 words; **revised**, 03/29/2017]

Network-based approaches that exploit inferred transcription factor activity to analyze the impact of genetic variation on gene expression

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ABSTRACT

Over the past decade, a number of methods have emerged for inferring protein-level transcription factor activities in individual samples based on prior information about the structure of the gene regulatory network. We discuss how this has enabled new methods for dissecting trans-acting mechanisms that underpin genetic variation in gene expression.

KEYWORDS

gene regulatory networks; transcription factor activity; systems genetics; QTL mapping

FUNDING

This research was funded by National Institutes of Health grant R01HG003008.

HIGHLIGHTS

- Large-scale compendia of parallel genotype and molecular phenotype data are creating new opportunities for dissecting regulatory networks.
- The activity of transcription factors can be inferred by integrating prior information about their DNA binding specificity with genome-wide information on transcript abundance.
- Treating inferred transcription activity as a quantitative trait provides a powerful strategy for mapping *trans*-acting genetic determinants of gene expression variation.
- Linear regression methods can be used to perform sophisticated transcription-factor-centric analyses, *e.g.*, mapping genetic polymorphisms associated with co-factors that modulate the responsiveness of the cell to perturbation.

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