

Phenomic profiling of *E. coli*

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Phenotypic Landscape of a Bacterial Cell

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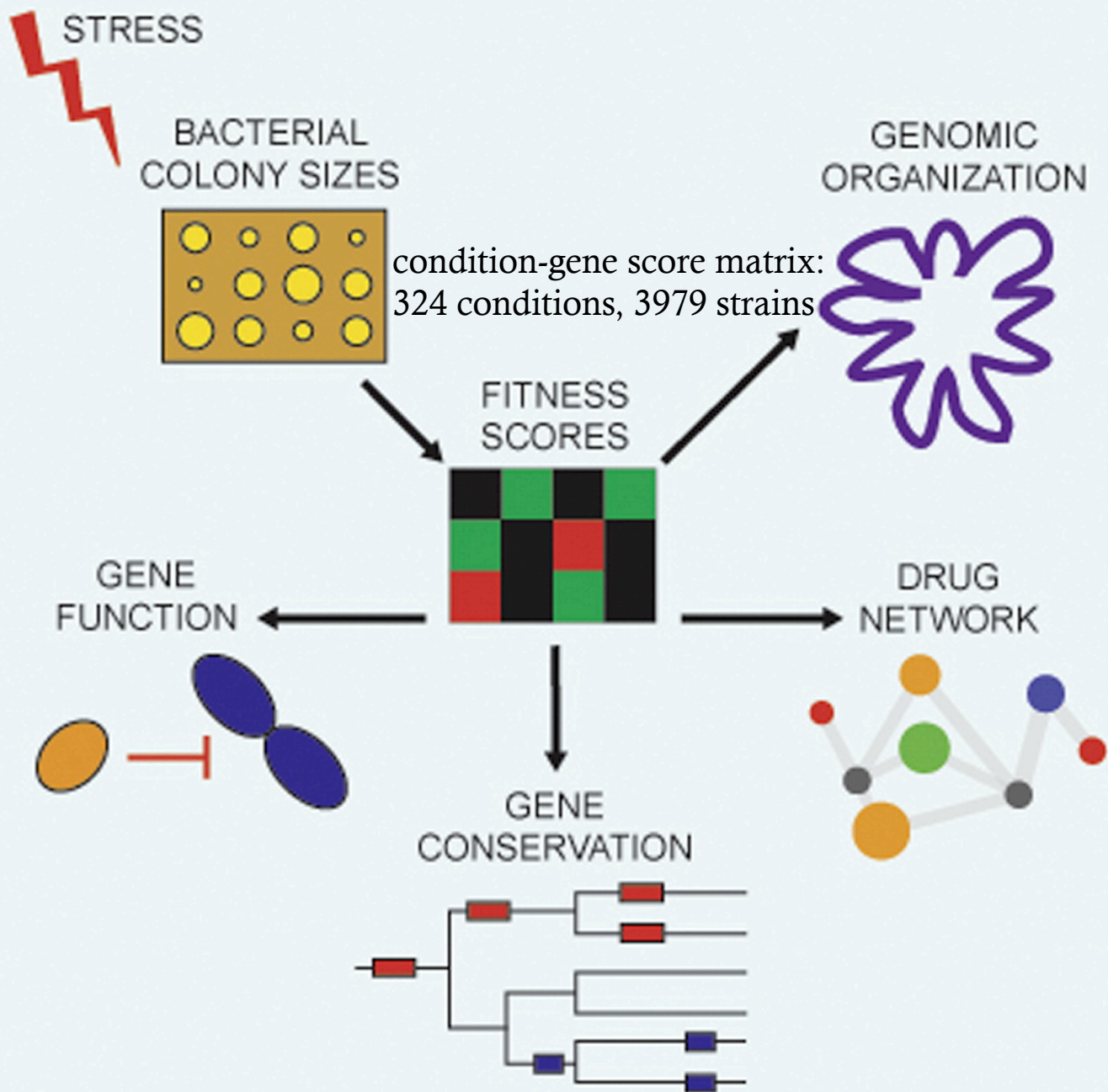
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Examples of conditions

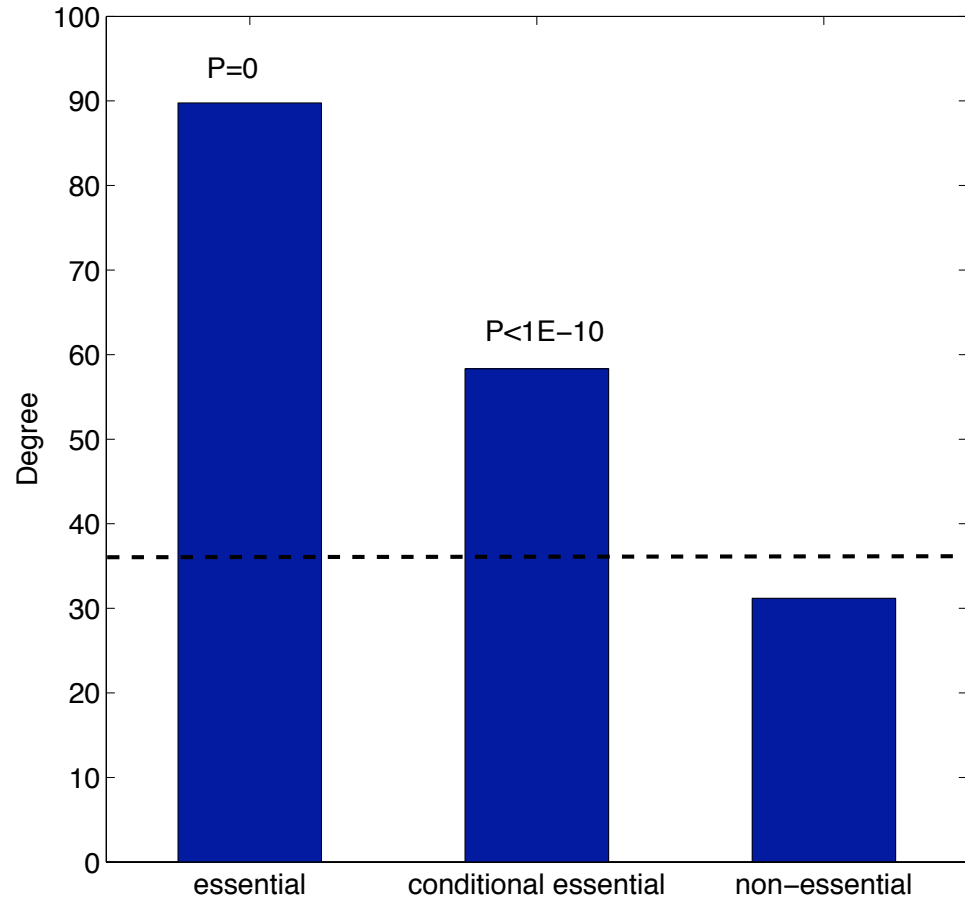
| | | |
|-------|-----------------|--------------------|
| 16C | BENZALKONIUM-1 | GENTAMICIN-0.05 |
| 18C | BENZALKONIUM-10 | GENTAMICIN-0.1 |
| 20C | BENZALKONIUM-25 | GLUCOSAMINE |
| 40C | BICYCLOMYCIN-1 | GLUCOSE |
| 42C | BICYCLOMYCIN-10 | GLUFOSFOMYCIN-0.05 |
| 43.5C | | GLUFOSFOMYCIN-0.2 |
| 45C | OXACILLIN-0.5 | GLYCEROL |
| | OXACILLIN-40.0 | |
| | OXACILLIN-5.0 | |
| PH10 | PARAQUAT-0.2 | UV-12SEC |
| PH4 | PARAQUAT-1.0 | UV-18SEC |
| PH4.5 | PARAQUAT-10.0 | UV-24SEC |
| PH5 | PARAQUAT-18.0 | UV-6SEC |
| PH6 | PARAQUAT-5.0 | |
| PH8 | PEROXIDE-0.1 | |
| PH9 | PEROXIDE-0.5 | |
| PH9.5 | PEROXIDE-1.0 | |
| | PEROXIDE-2.0 | |

Several novel concepts

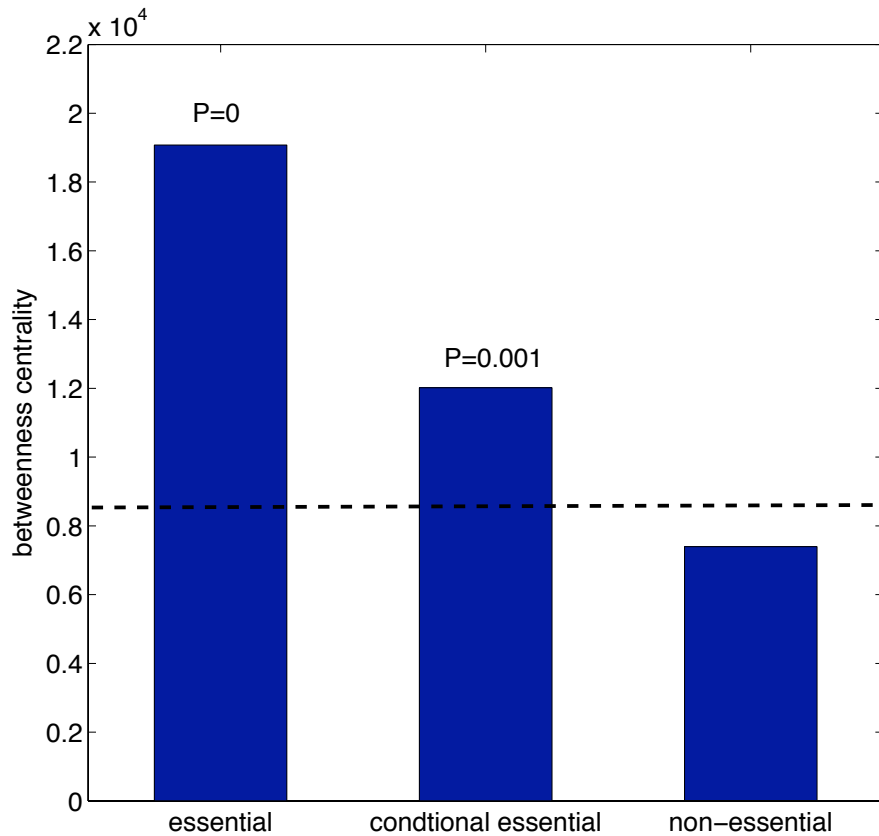
- ⊗ Responsive genes (1957 strains)
- ⊗ Multi-stress responsive genes (94 strains)
- ⊗ Conditional essential (116 strains)
- ⊗ Where are these guys located in various networks: PPI, transcription regulatory network, metabolic network?
 - ⊗ e.g. MSR genes tend to be hubs in PPI (deg=62.9, cf 36.4)

Essentiality versus centrality

PPI network for *E. coli*
4100 nodes, 75000 edges
(Hu et.al. PLoS Biol 2009)



Essentiality versus centrality



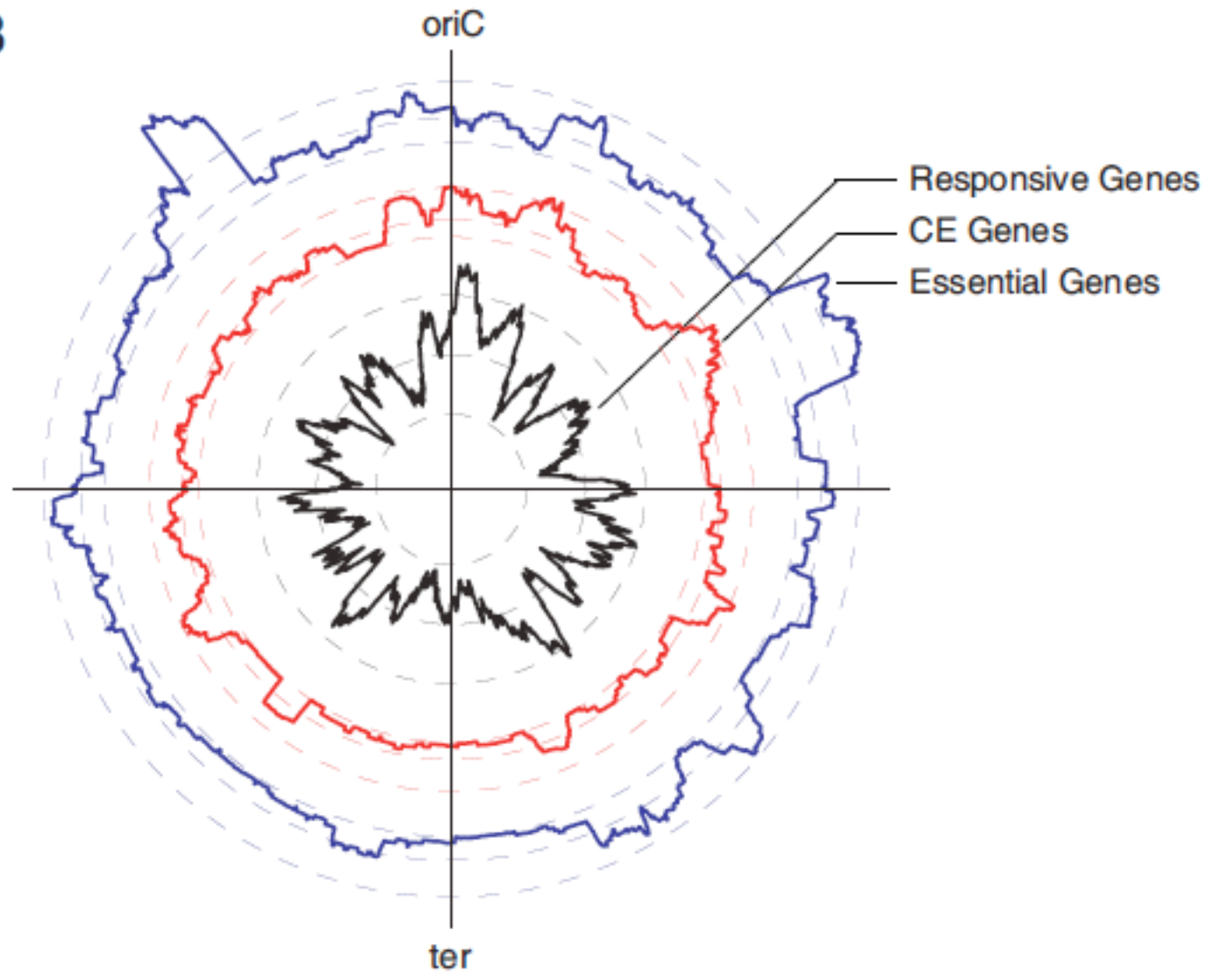
conditional essential



Non-essential

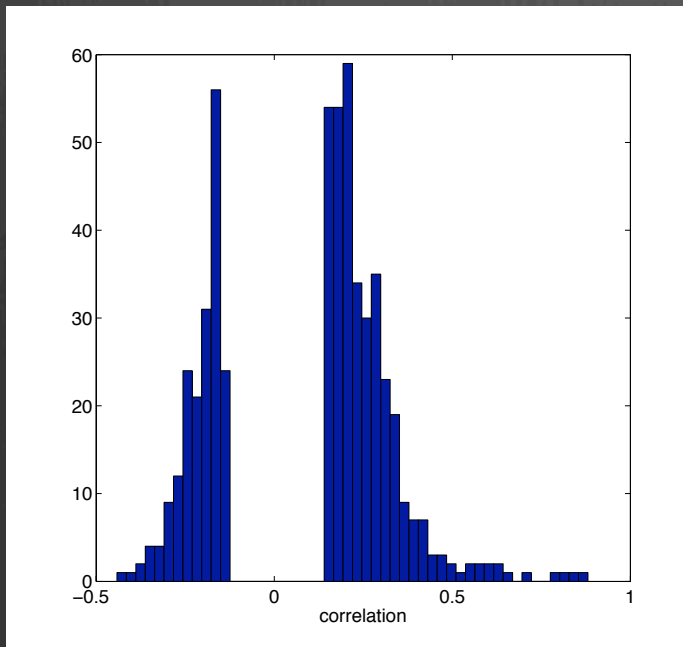
Essential

B



Phenotypic signatures of regulator and target pairs

- The knockout of TFs shows weaker phenotypic response
 - Out of 224 TFs, only 6 of them are conditional essential, and 4 are MSR
 - Making use of RegulonDB, 2600 TF-target pairs, only 540 pairs show significant correlation between the signatures



Signs of correlation NOT entirely agree with signs of regulatory interactions

Next steps

- ⊗ Group enzymes into pathways, and look at the effects of TF knockouts on pathways
- ⊗ A framework to assign TFs to different pathways. May be better, or at least complementary to look at the transcription regulatory network
- ⊗ Understand the regulation of metabolic activities

Noise

- ⊗ Taniguchi et.al. Science 2010: Single cells level protein abundance
- ⊗ MSR genes, conditional essential genes, and essential genes are less noisy in general
- ⊗ Where are the noisy guys? Are they responsive to different conditions?