How noisy is *E. coli*? (update)

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Nets
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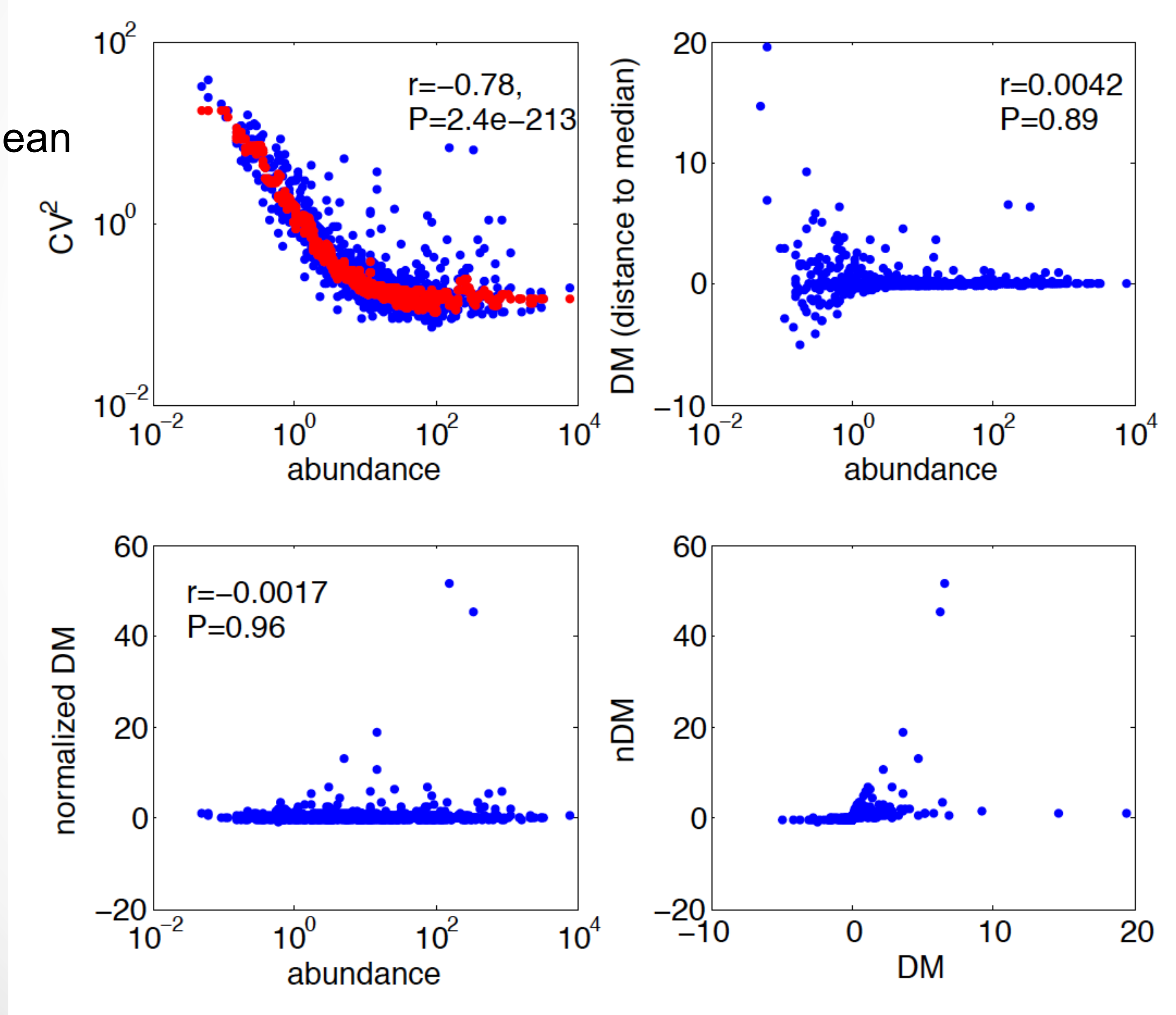
Genetic approach to noise

- Understand from a system-wide standpoint why certain genes are more noisy or quiet (variation of protein abundance in a population of cells)
- How noise is being controlled or exploited?
- Noise versus the organization of networks
  - *E. coli*
  - PPI: Proteins forming complexes are less noisy
  - No apparent correlation between the transcription regulatory network and noise (NOT the case in yeast)

Various noise metrics

CV=std/mean



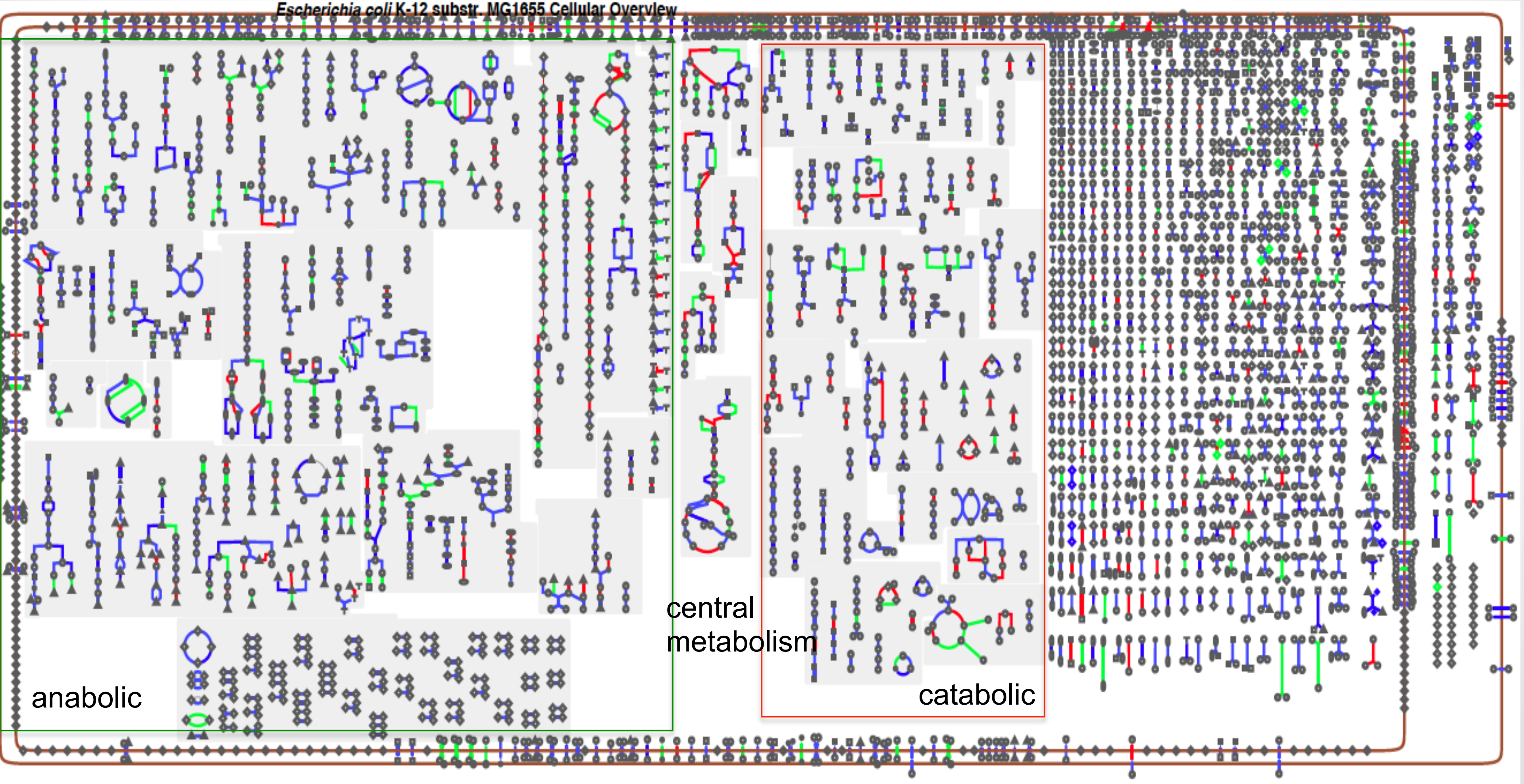
Annotated Pathways

- Biocyc (Ecocyc)
- 361 annotated pathways
  - Biosynthesis (177)
  - Degradation (124)
  - Detoxification, Acid-Resistance, Antibiotic-Resistance (9)
  - Signaling (28)
  - Respiration, Energy-Metabolism, Fermentation, GLYCOLYSIS, TCA, Nitrate-Reduction, Electron-Transfer, Pentose-Phosphate-Cycle (26)
- Yeastcyc, 154 pathways
- Human, mouse, …

Noise in individual pathways

Biosynthesis:
enriched with quiet guys (P=0.05)

Detoxification: enriched with noisy guys (P=0.05)
Degradation: enriched with noisy guys (P=0.0064)

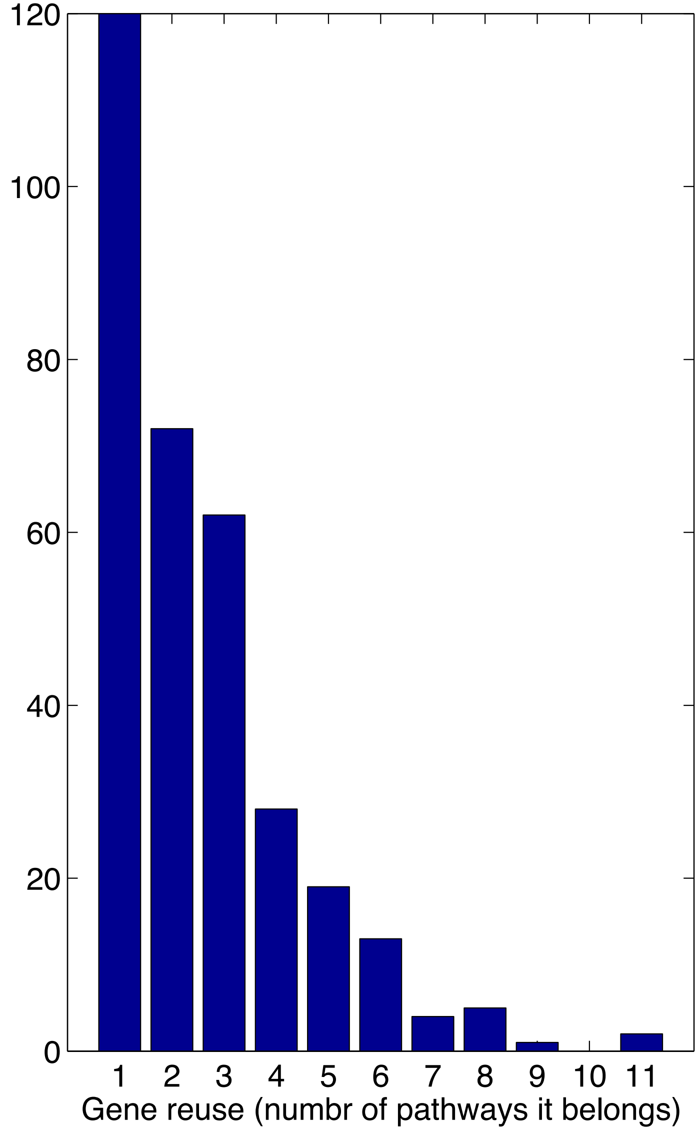


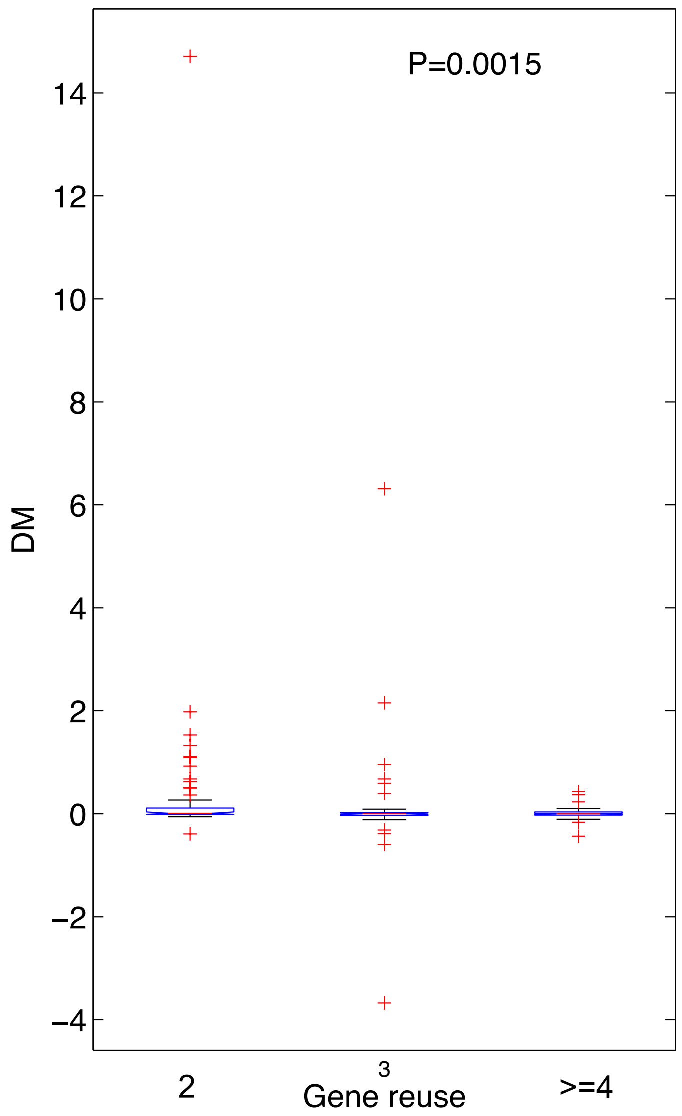
red: noisy, blue: middle, green: quiet

Possibilities

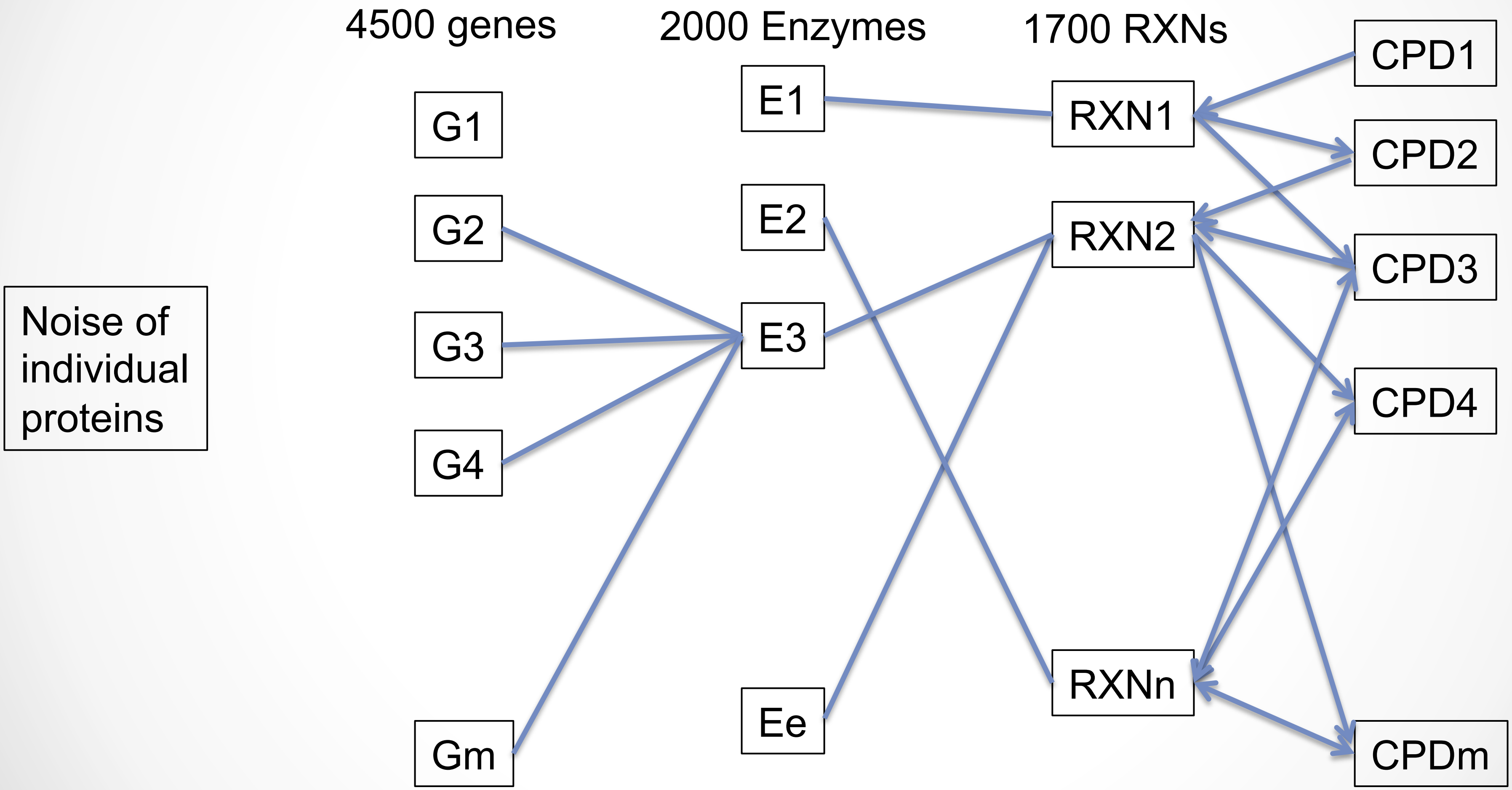
- Genes in direct response to outside world are more noisy. A strategy to adapt to fluctuations in outside world, instead of incorporating a sophisticated sensory system. This is consistent to the noisy nature of detoxification pathways
- Synthesis involves genes that more less noisy. It is a waste to synthesize too much, or it’s lethal to synthesize too little

Gene reuse versus noise





Integration of Biocyc (Ecocyc) information



Noise of individual proteins

4500 genes

G1

G2

G3

G4

Gm

2000 Enzymes

E1

E2

E3

Ee

1700 RXNs

RXN1

RXN2

RXNn

CPD1

CPD2

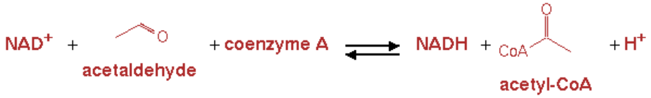
CPD3

CPD4

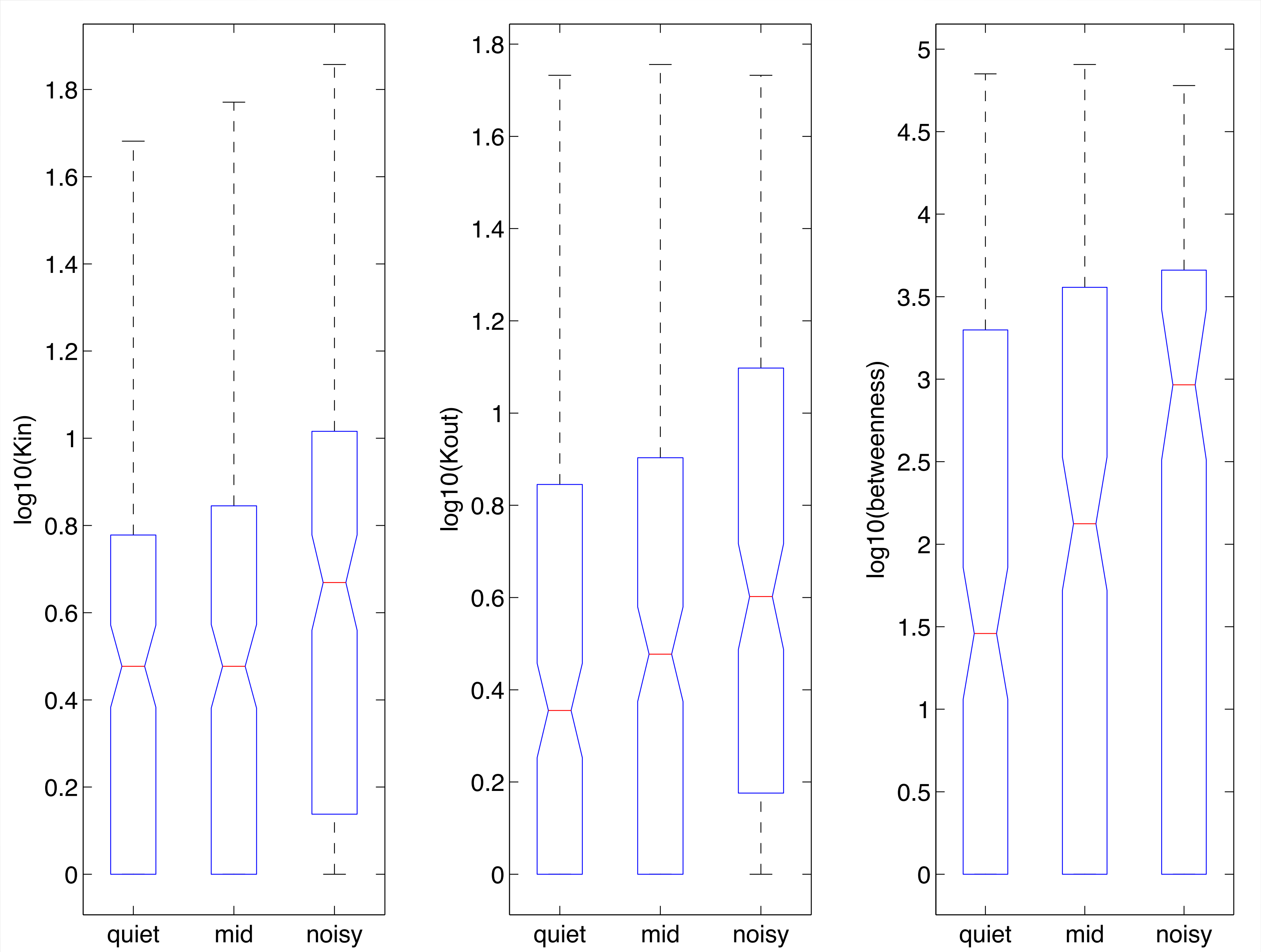
CPDm

Reaction Network (integration of pathways)

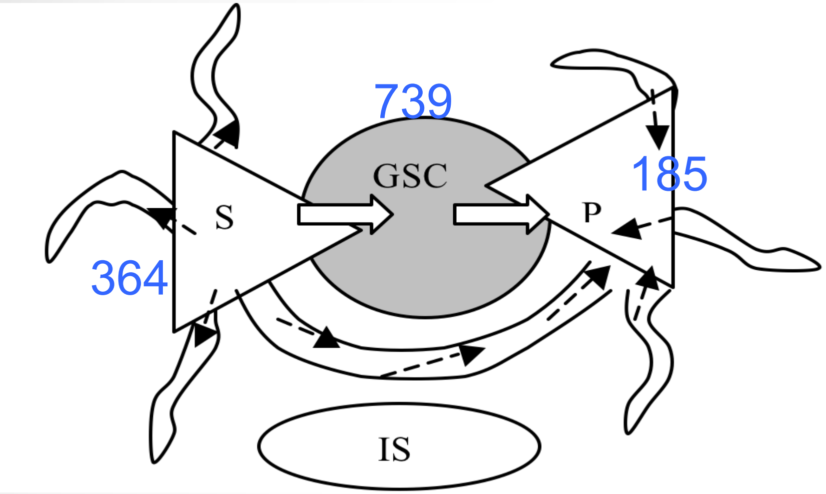
- Most reactions are used in only 1 pathway, the maximum reuse is 6

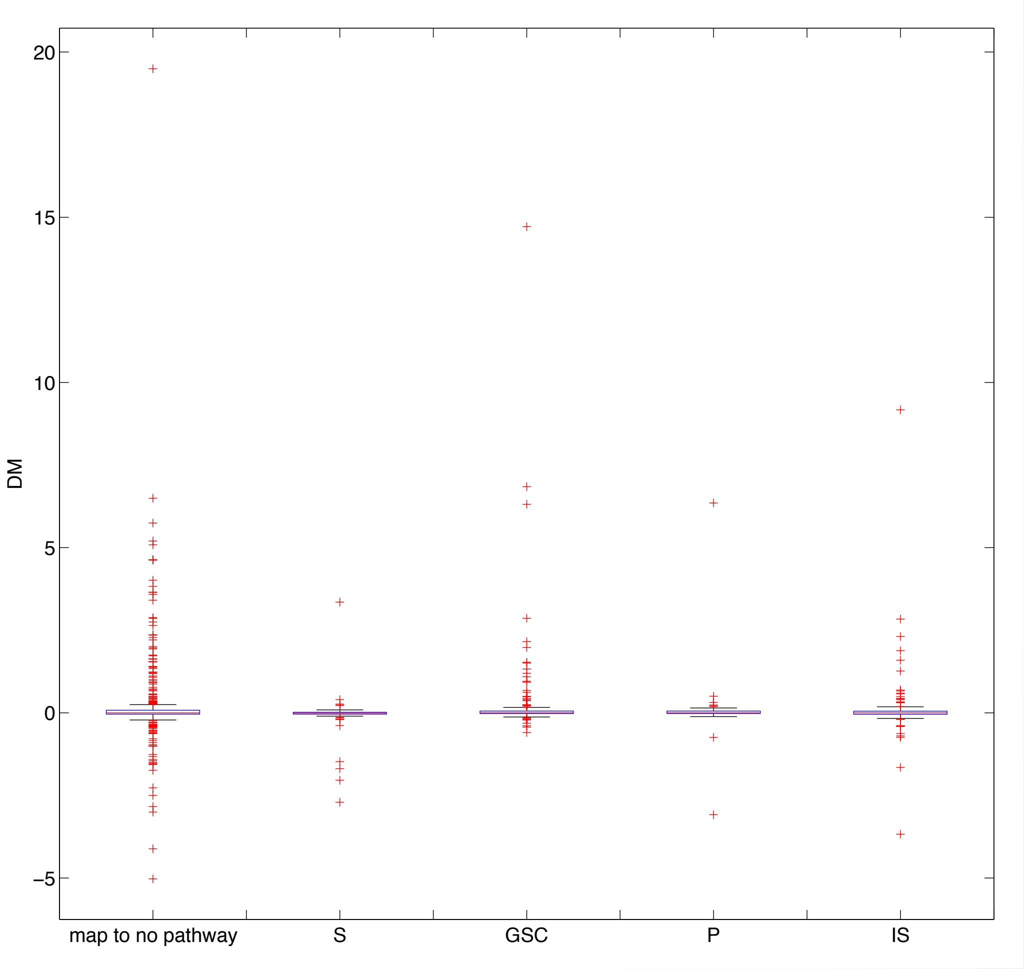


- A->B if a product of A feeds as an input to B
- 1662 nodes, 216500 edges, deg(in-hub,out-hub)~ 600, SCC~76%
- Compounds in many reactions: H+, H2O, ATP, ADP, phosphate, diphosphate, CO2, NH3, O2, NAD, NADP, NADH, NADPH
- 9856 edges, deg(in-hub)~70, deg(out-hub)~60, scc~45%


log10(Kin)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
quiet
mid
noisy
log10(Kout)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
1.8
quiet
mid
noisy
log10(betweenness)
0
0.5
1
1.5
2
2.5
3
3.5
4
4.5
5
quiet
mid
noisy

Components of the reaction network





Summary, and …

- A basic understanding of using Biocyc
- Map noise information of E. coli to system-wide networks
  - metabolic pathways
  - Pathways responsible for degradation are noisier
  - Central guys are noisier?
- Incorporate more knowledge from biochemistry, what kind of biosynthesis?
- Metabolic pathways analysis for yeast, any difference between E. coli and yeast