Tuning noise in global gene expression

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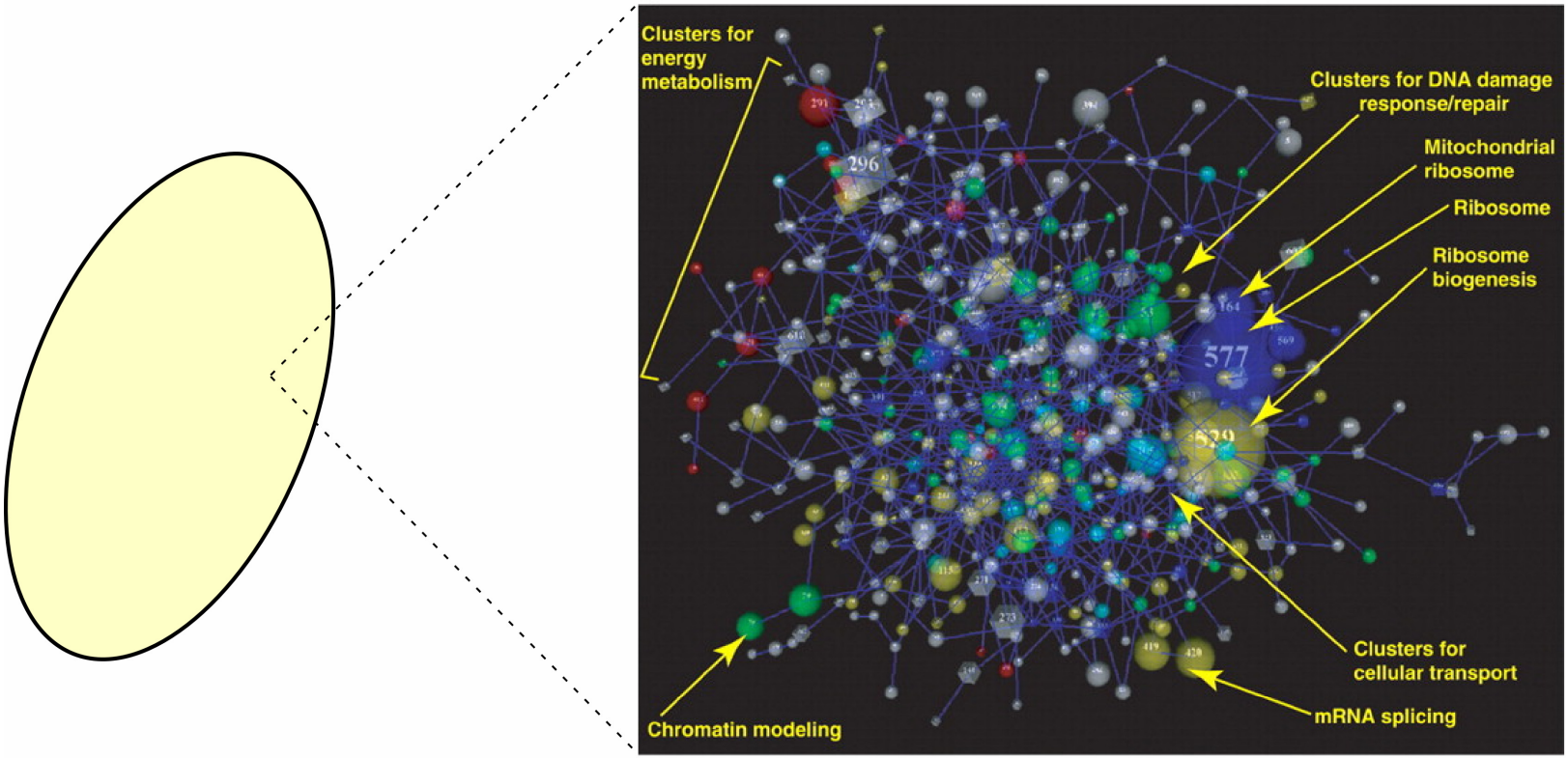
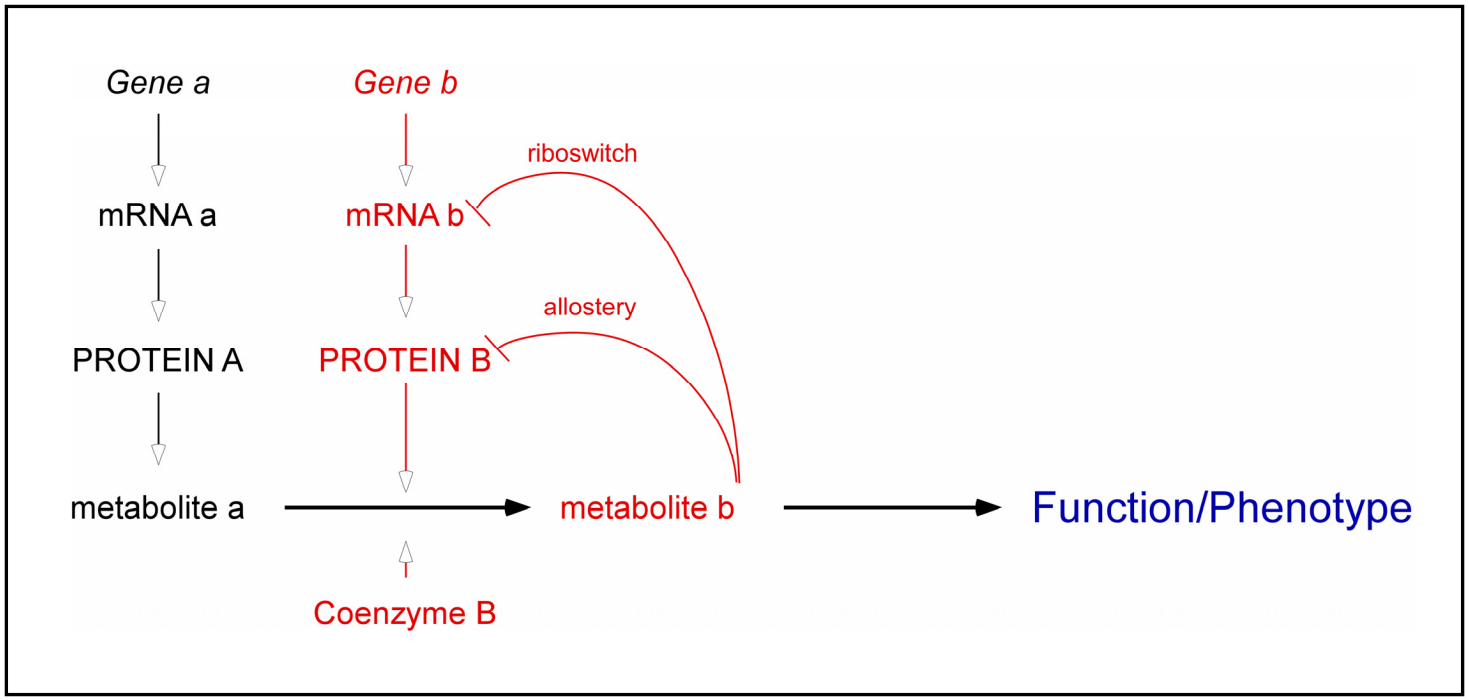
ICSB 2005

Cells are made of complex networks

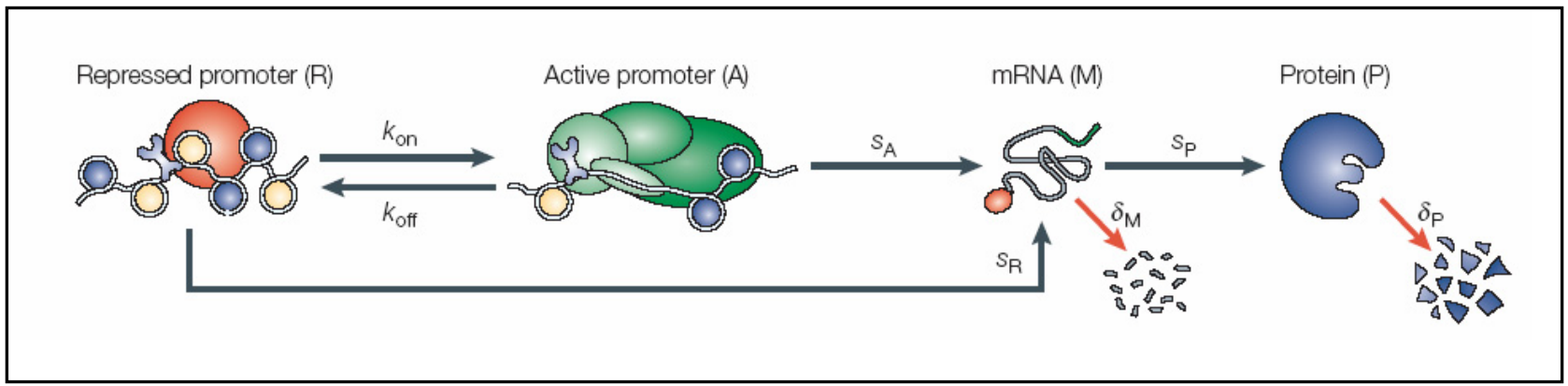


Adapted From: Lee et al., *Science*, 2004

Complex networks are made of simpler modules



Gene expression is a random probabilistic process



Random events become significant:
Small numbers of molecules whose state is amplified into a larger signal

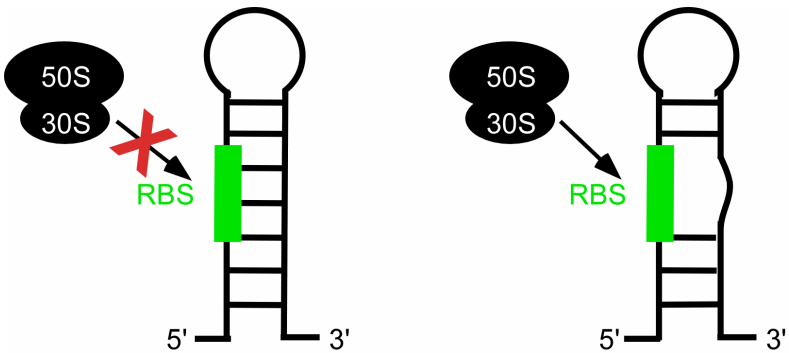
Noise hypothesized to be dependent on global factors:

- Polymerases
- Ribosomes

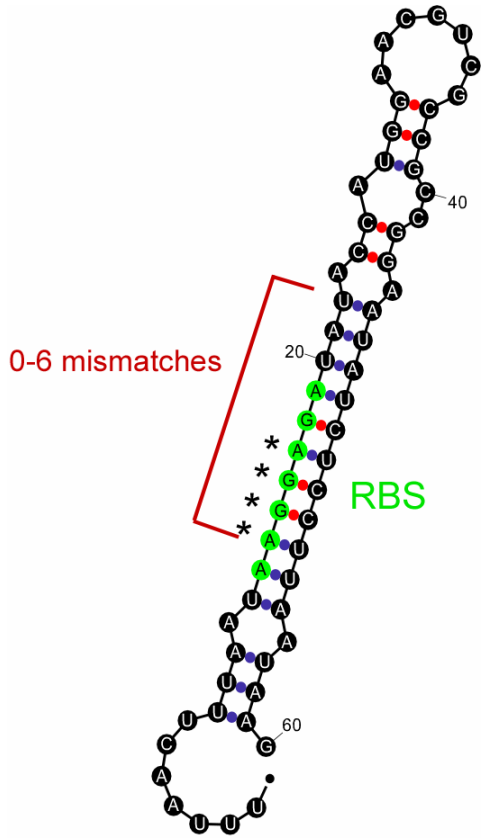
From: Kaern et al., *Nature Reviews Genetics*, 2005

How does translational capacity affect noise?

strategy

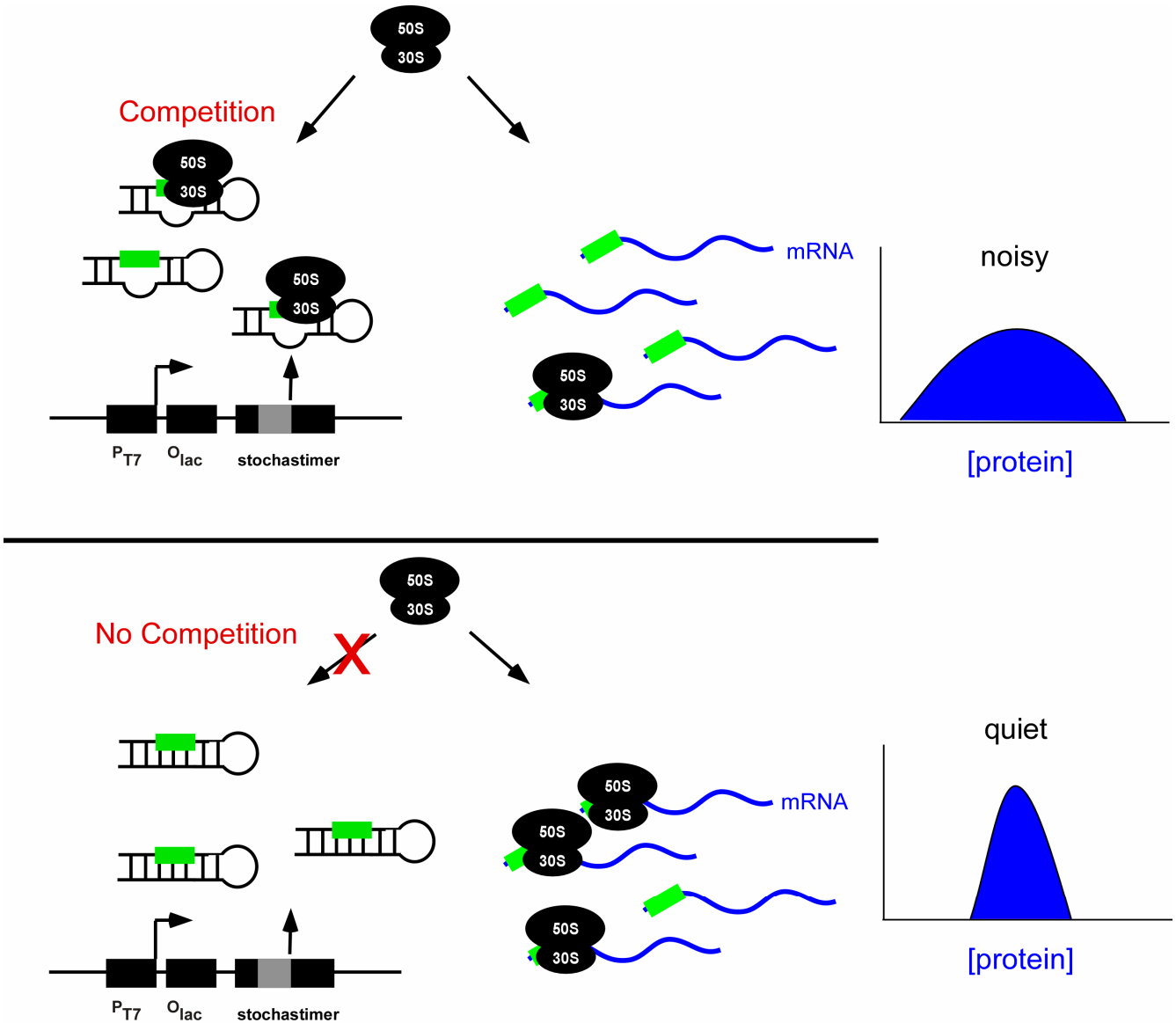


"stochastimer" anatomy

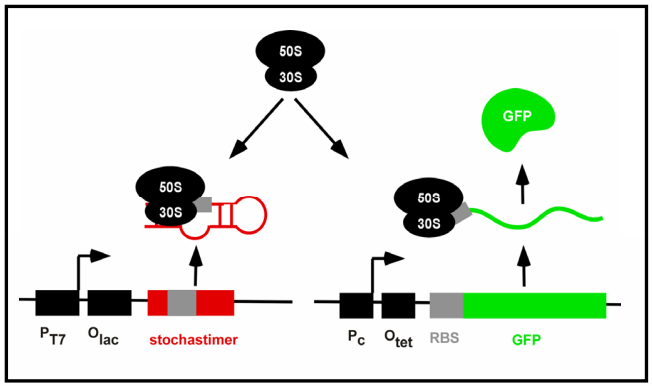


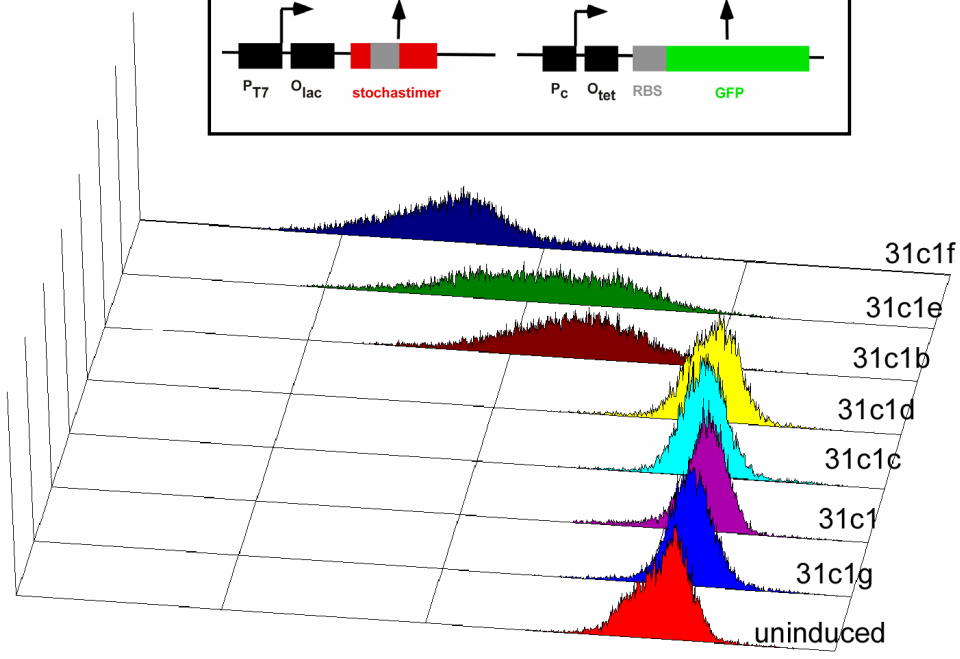
http://www.bioinfo.rpi.edu/applications/mfold/old/rna/

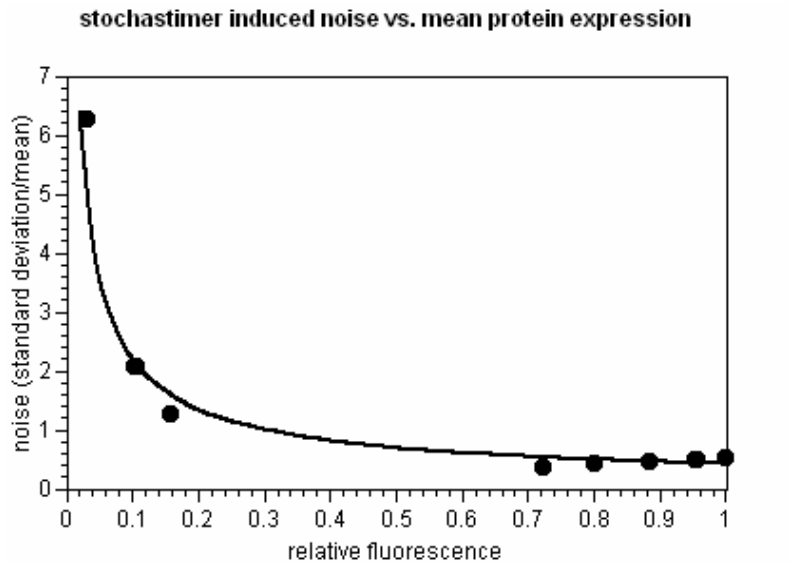
Competition for translation machinery



Stochastimers tune noise in gene expression

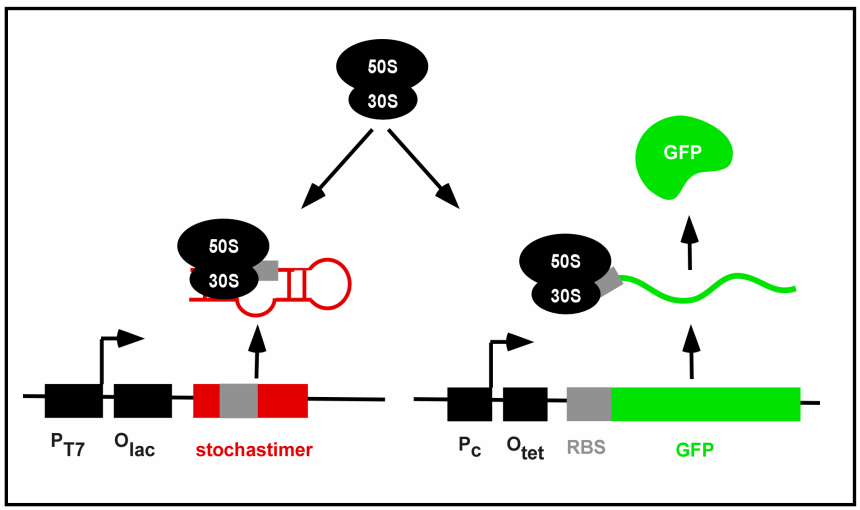


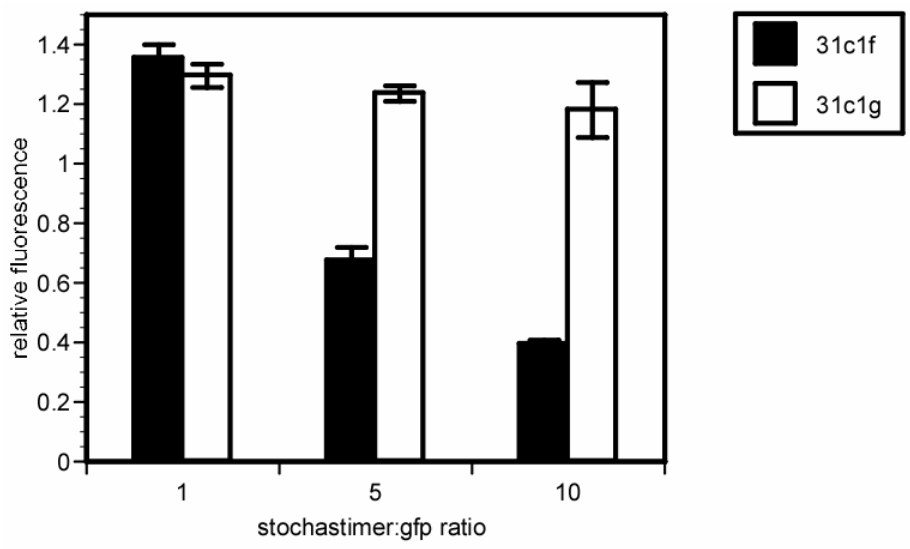


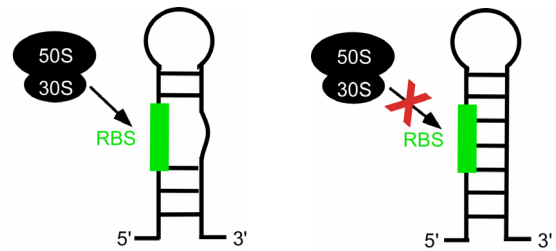


Stochastimers directly compete for translation machinery

Assay:
- *in vitro* translate GFP
- Titrate in stochastimer
- Monitor translation capacity

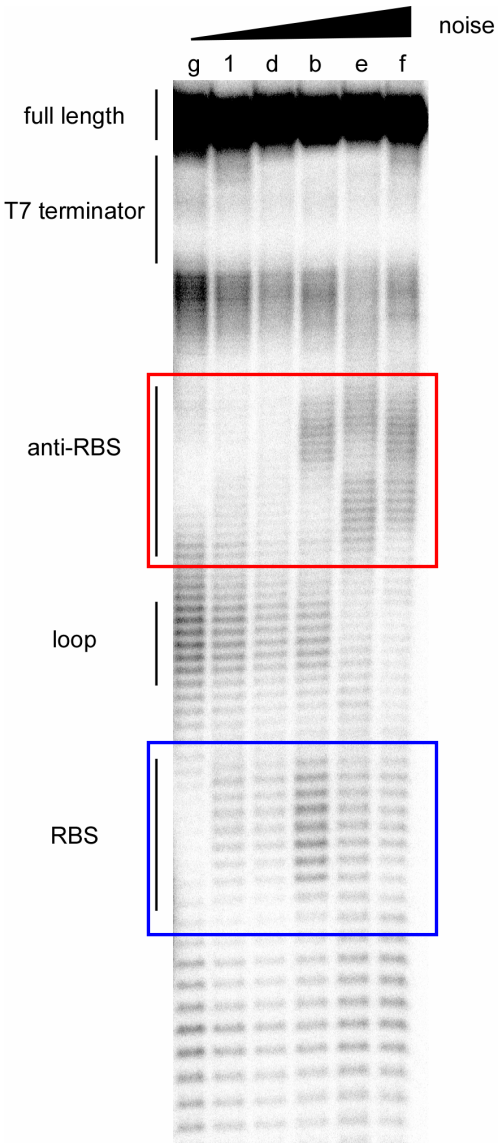


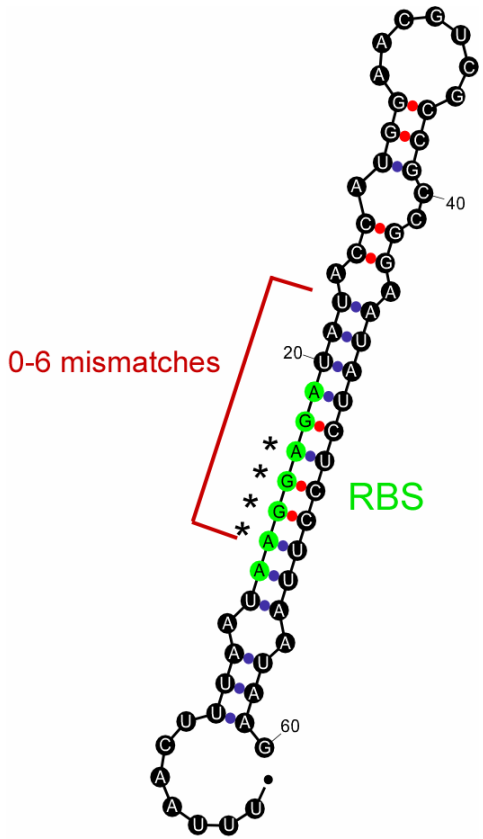




31c1f 31c1g

Structure mapping confirms function

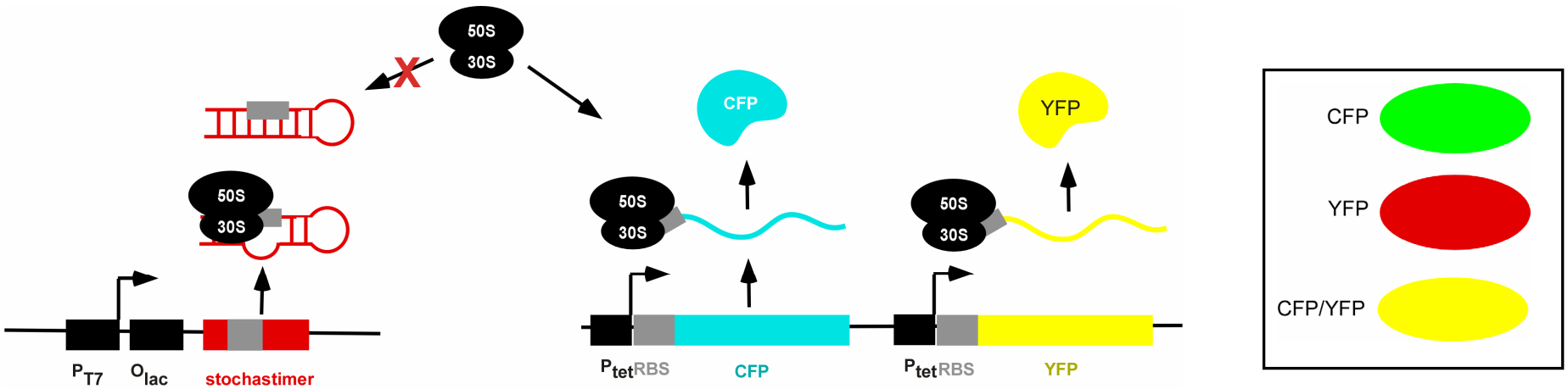




“G”

Two gene correlation assay

- Fluctuations in mRNA levels suspected to be responsible for most noise
- Bicistronic encoding (operons) predicted to decrease noise in the expression of 2 genes (Swain, 2004).

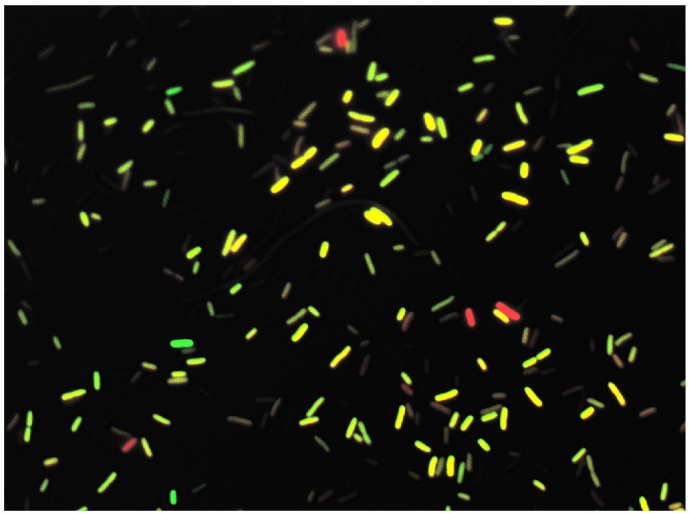


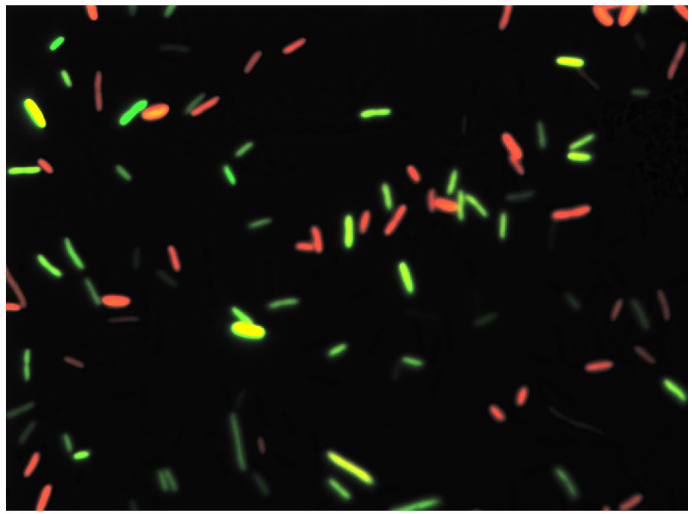
Stochastimers predictably de-correlate monocistronic genes

wild-type

noisy

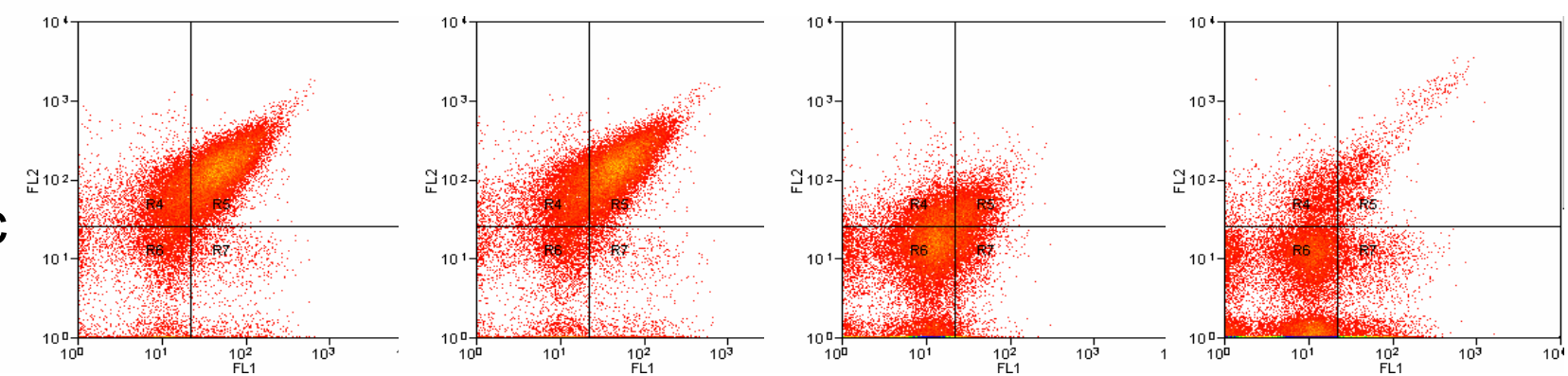
mono-
cistronic



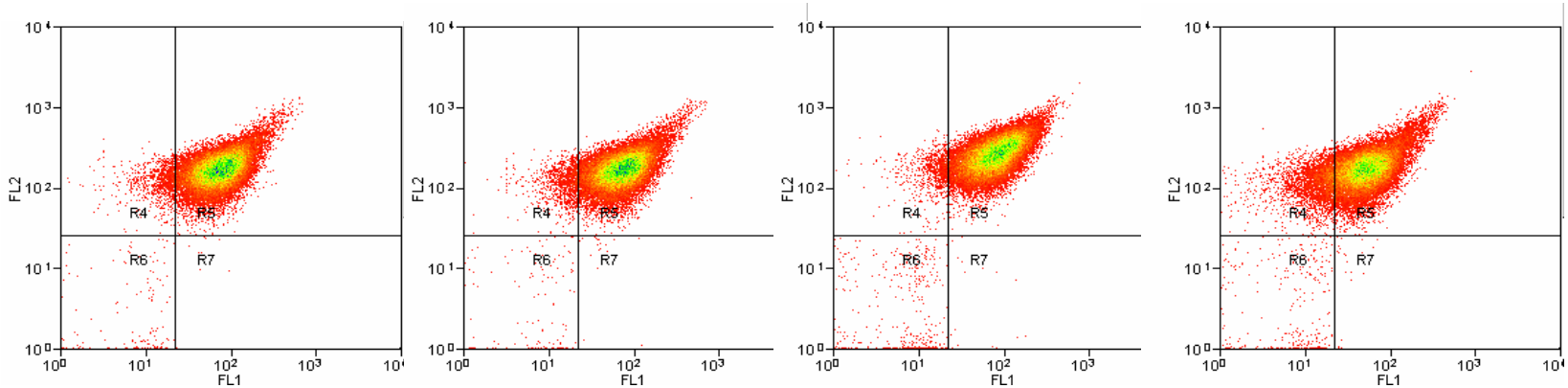


Operons are genetic noise insulators

Mono-cistronic



Bi-cistronic



Wild-type

noise

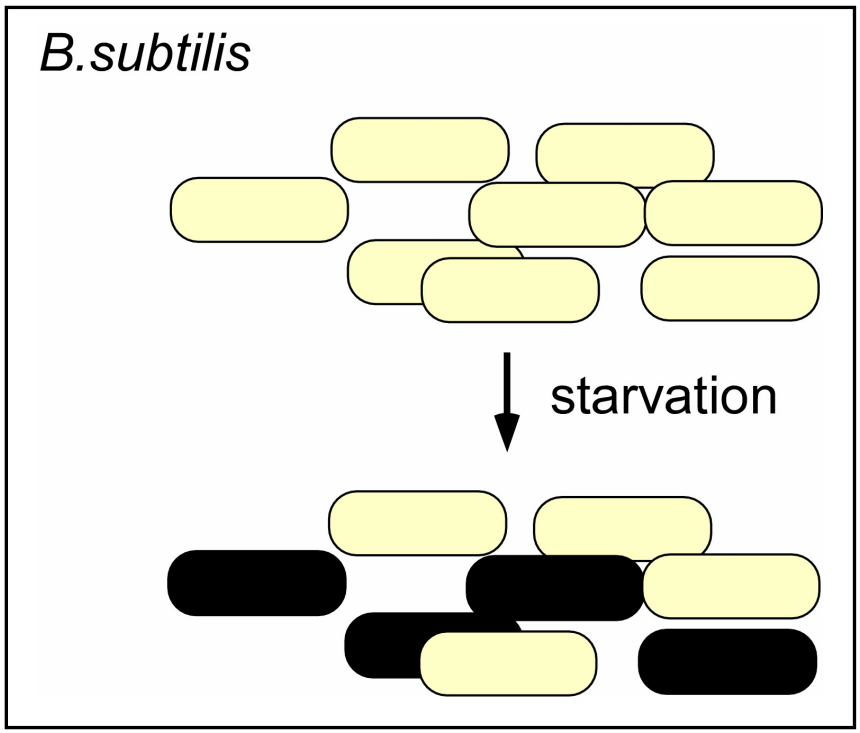
Conclusions

- Translation machinery significantly affects noise in gene expression
  - Finite-number effects may explain this phenomenon
- Operons increase genetic correlation
  - Fluctuations in mRNA level and probabilistic ribosome:mRNA interaction likely strong noise determinant
- Operons insulate genes against large amounts of artificial noise

Acknowledgements

- **Travis Bayer**
- Andy Ellington
- Matt Levy
- Karl Griswold
- Zack Simpson

Evolution has taken advantage of noise



- Phenotypic variability. Sample more phenotype space with same genotype space
- Mechanism regulating sporulation in B.subtilis is stochastic (Maughan and Nicholson, *J.Bacteriology*, 2004)