

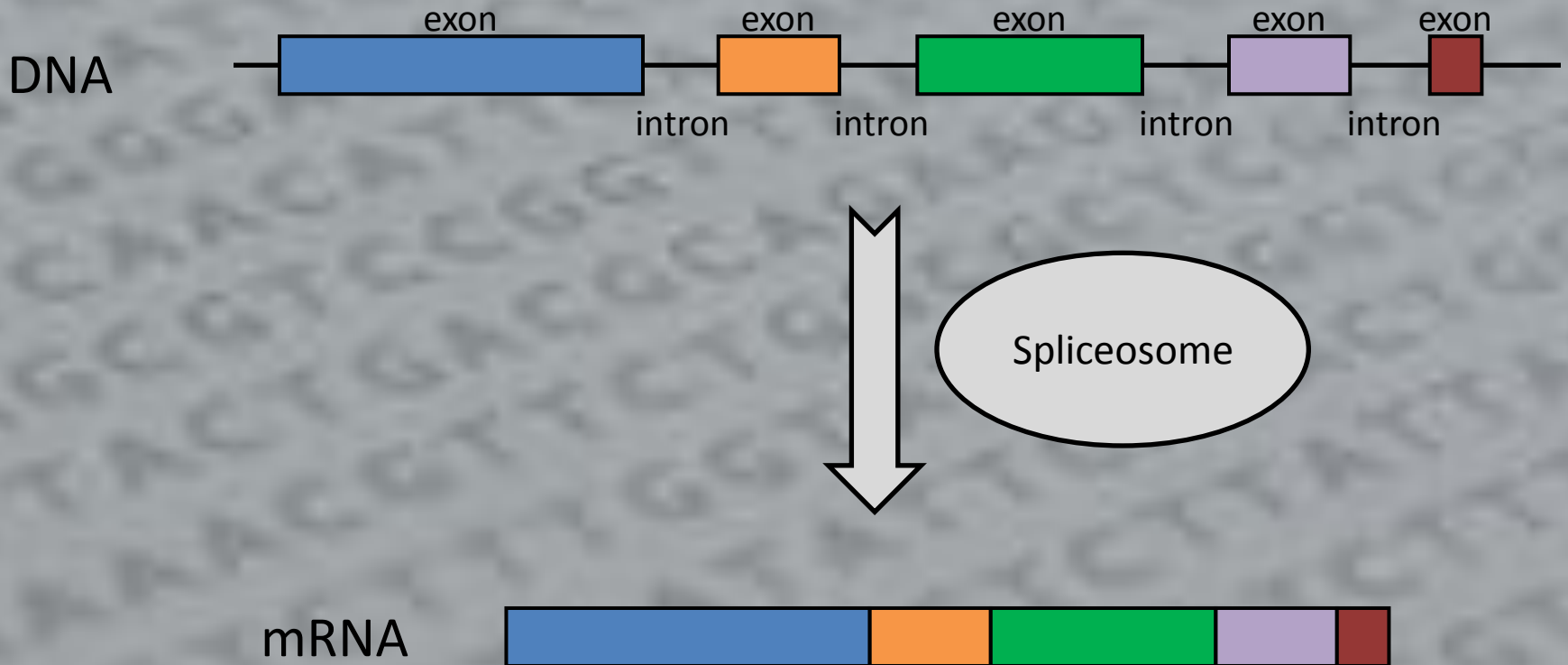
Traces of primordial eukaryotic mechanisms: the regulatory roles of the minor spliceosome

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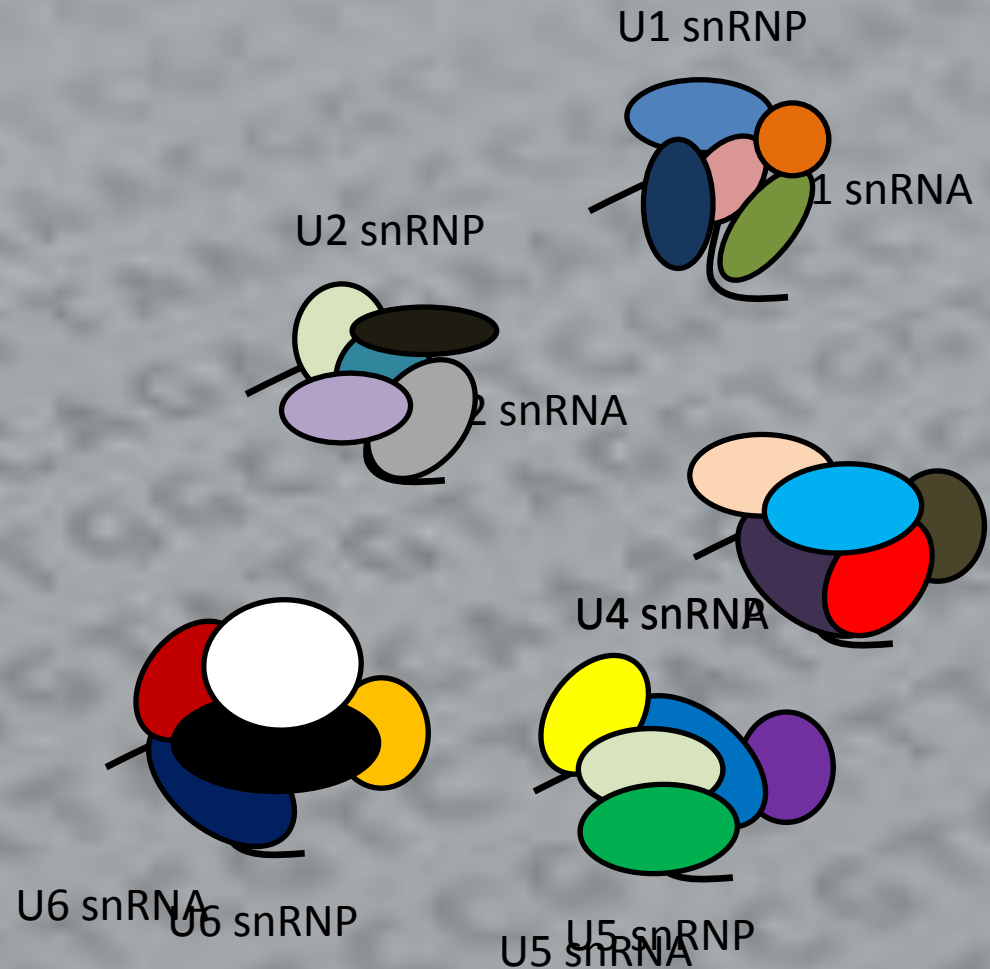
The Hebrew University of Jerusalem

Genes in pieces: the eukaryotic genomic organization

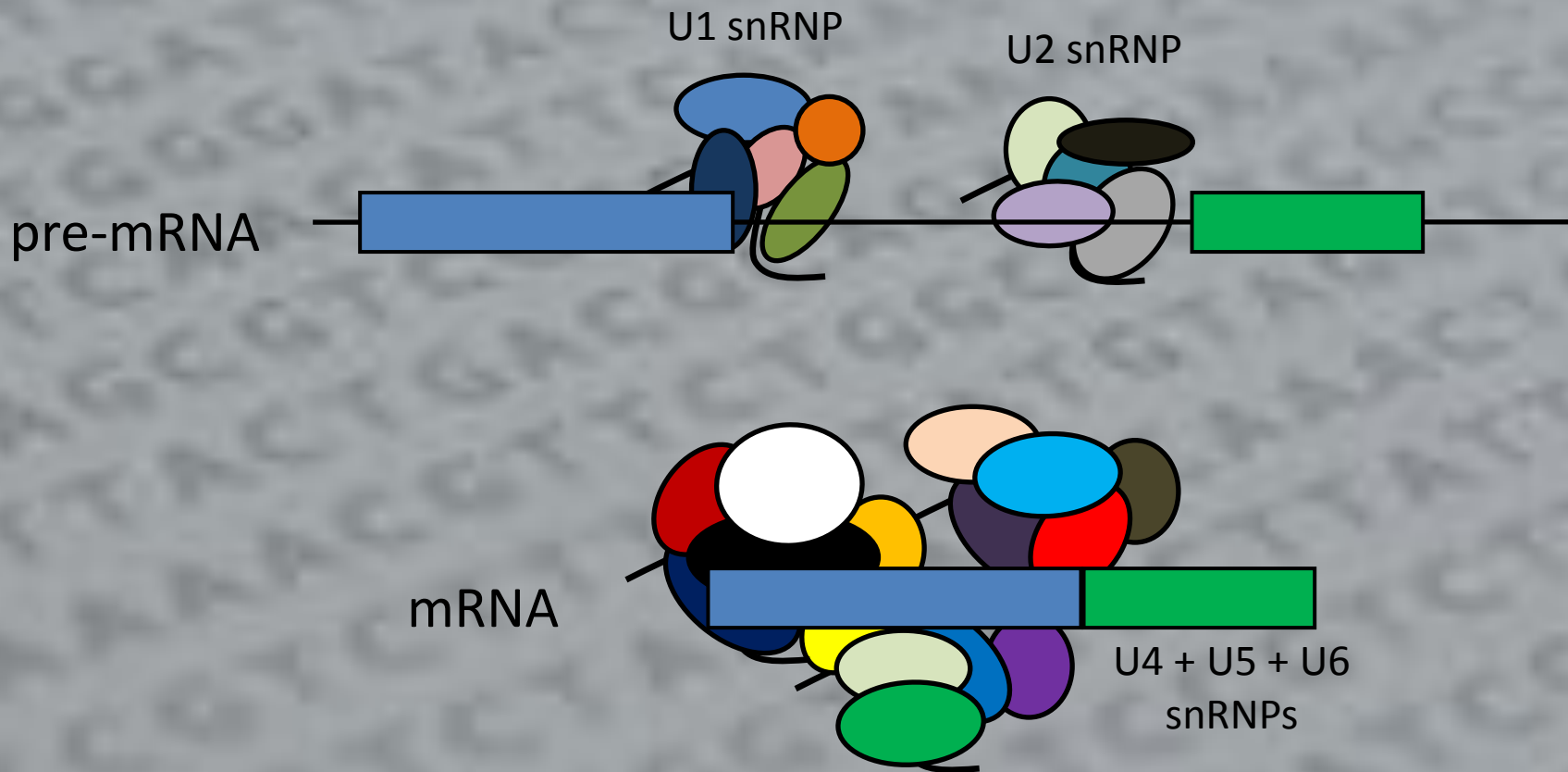


The spliceosome

- 5 snRNA genes
- Over 150 proteins
 - core U1, U2, U4, U5, U6 proteins
 - auxiliary proteins (splicing factors, transcription elongation, etc)



The spliceosome



The minor spliceosome

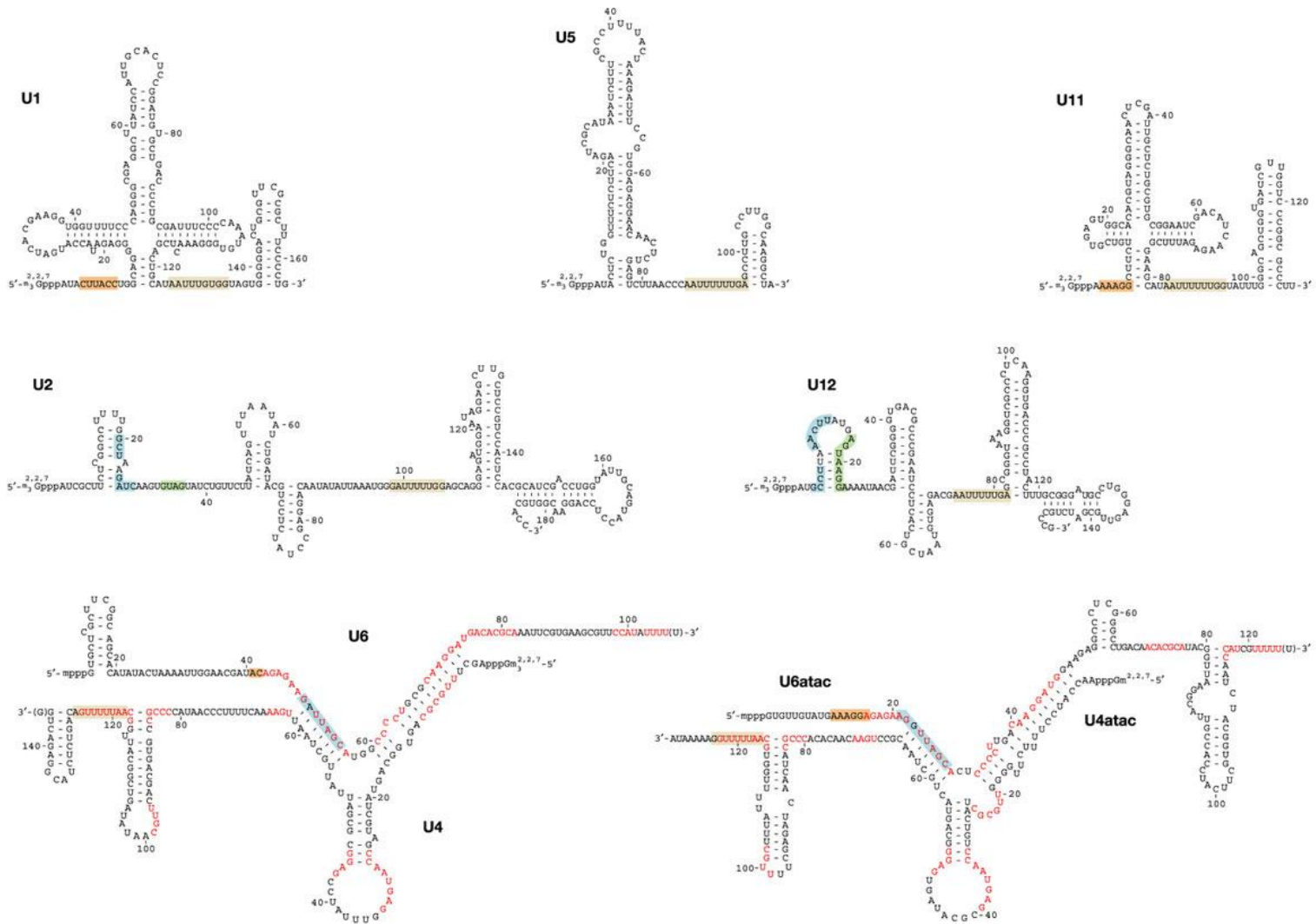


Figure taken from: A.A. Patel & J.A. Steitz (2003). Splicing double: insights from the second spliceosome. *Nature Reviews Molecular Cell Biology* **4**, 960-970.

The abundance of the minor spliceosome

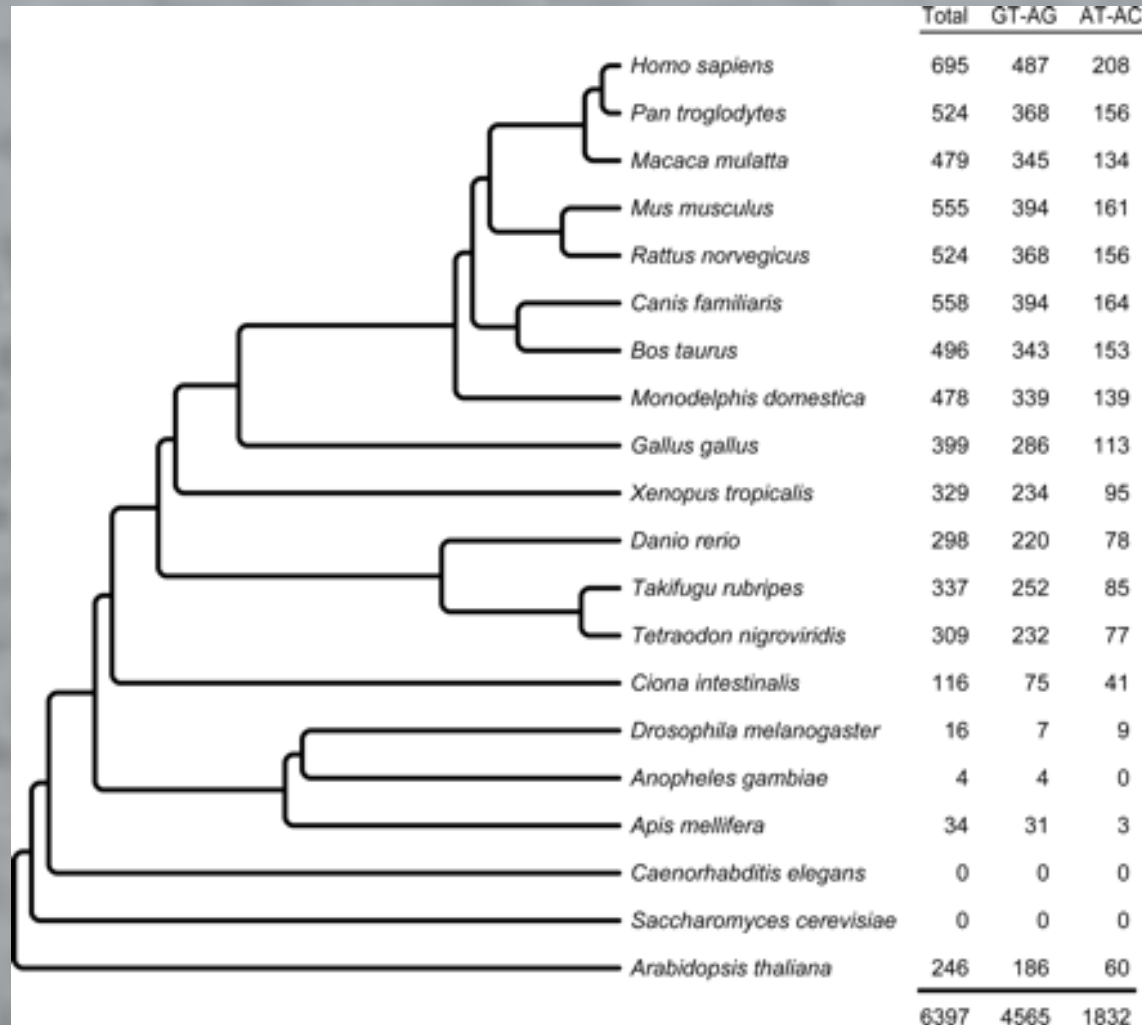
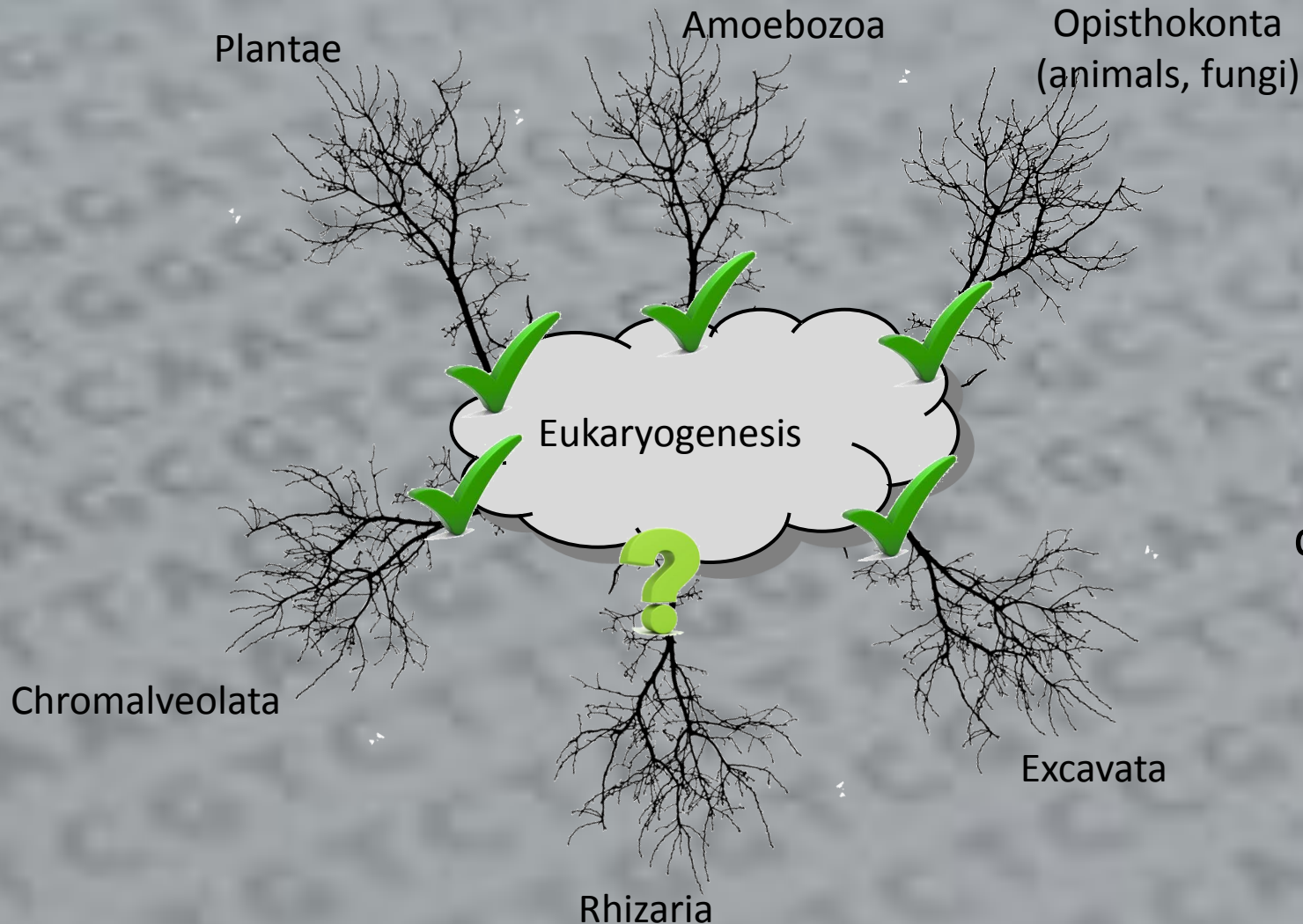


Table taken from: T.S. Alioto (2007). **U12DB: a database of orthologous U12-type spliceosomal introns**. Nucl. Acids Res. 35 (suppl 1): D110-D115.

Evolutionary history of the spliceosomes



U12 introns
show high
positional
conservation

Why did minor introns survive?

- Splicing of U12 introns is slower than that of U2 introns
 - U12 in endogenous pre-mRNAs in human show two- to nine- fold slower splicing
 - Mutating U12 to U2 in *Drosophila* increases the expression
- **The hypothesis:** U12 introns down-regulate the expression level of their host genes

Testing the hypothesis

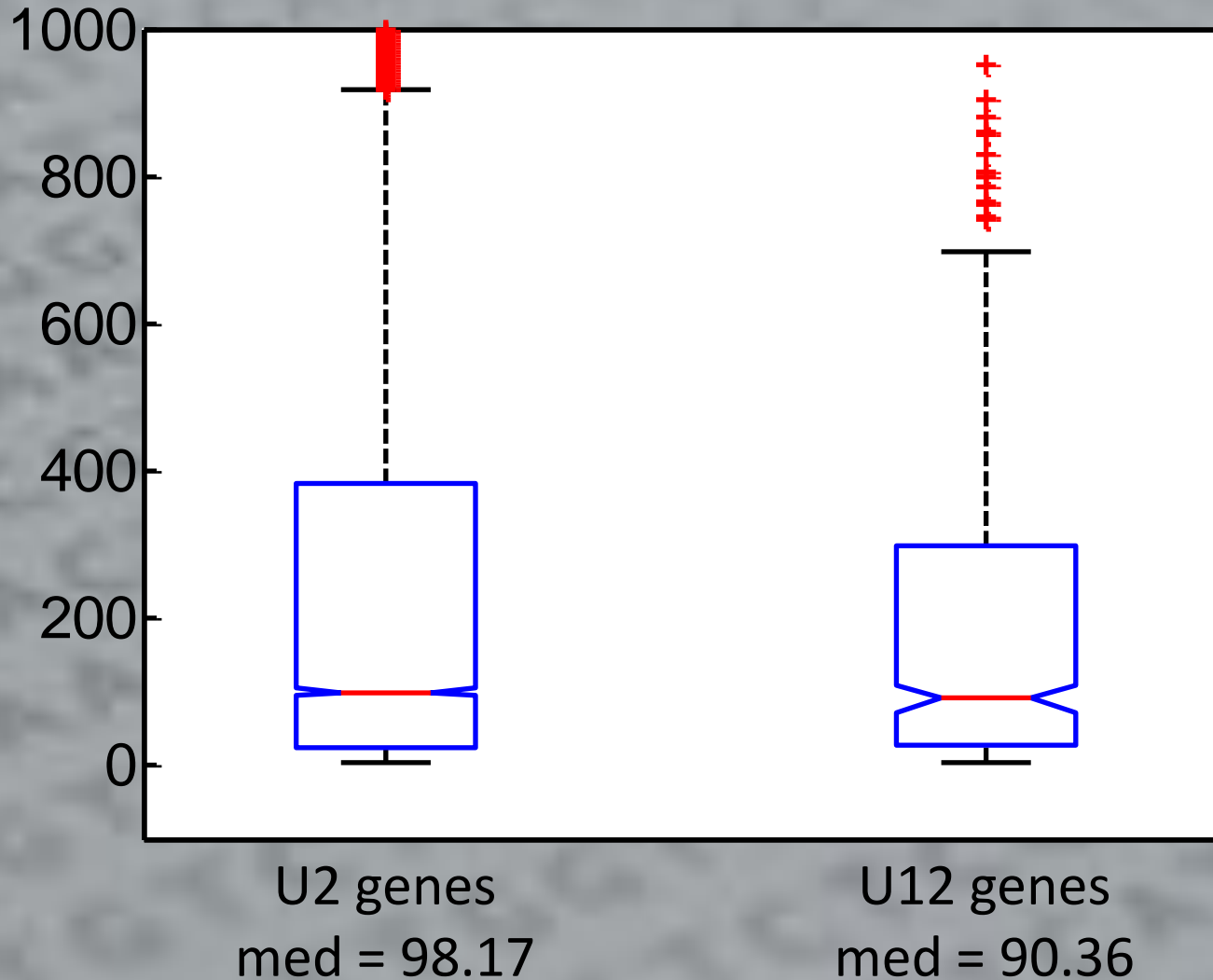
- Grouping human genes
 - U12 genes: have at least a single U12 intron
 - U2 genes: have introns, but none is U12
- Comparing the expression levels of the two groups

Data analysis

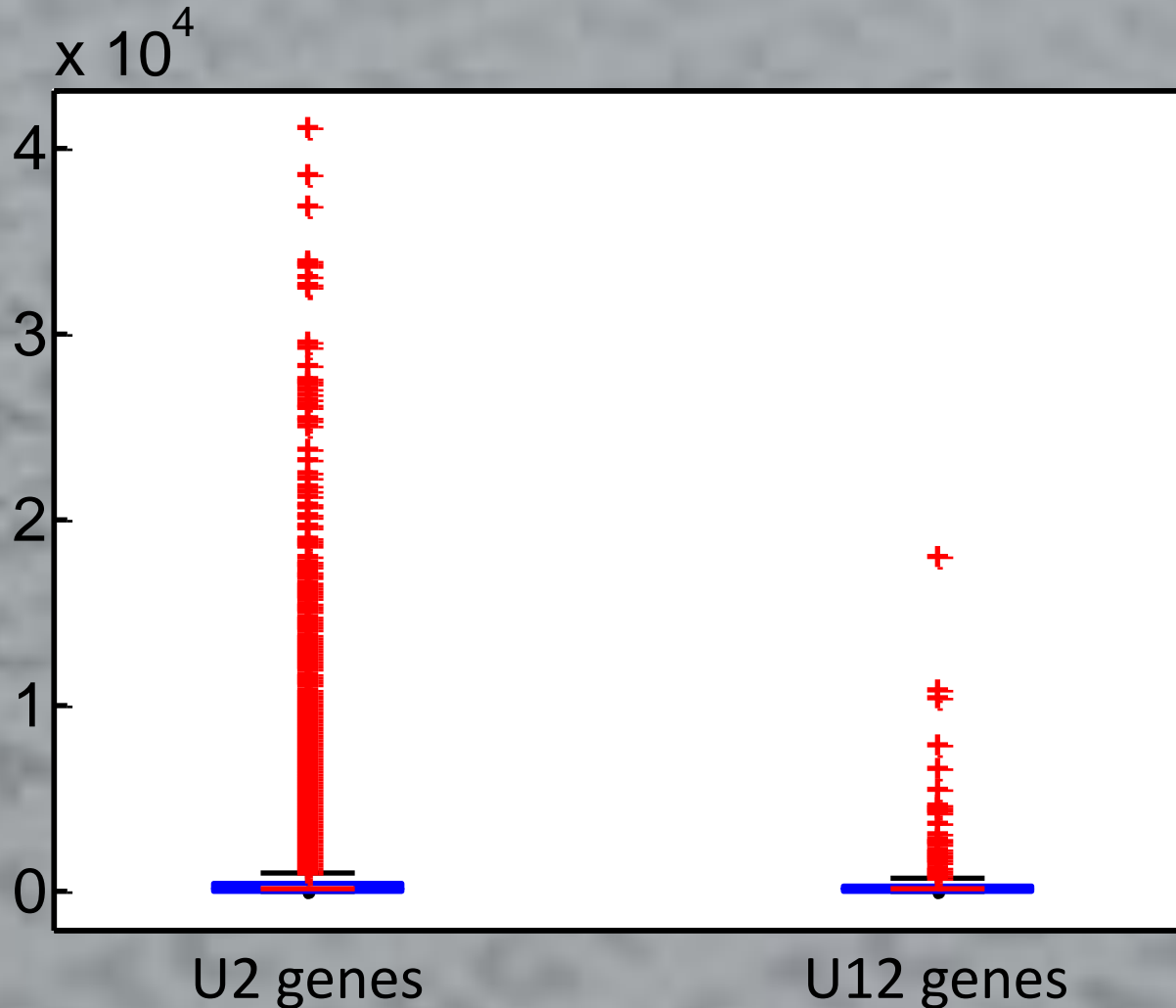
- Microarray expression measurements
 - 32 different tissues
 - 12,502 human genes
 - 503 U12 genes
 - 11,999 U2 genes

		tissues					
genes		2.7	13.2	10.1	3.9	...	
		12.3	13.7	13.8	12.9	...	
		10.6	4.4	4.2	3.7	...	
		3.1	3.0	18.5	20.0	...	U12 genes
		1.2	22.7	21.9	3.3	...	
		17.5	19.5	18.5	20.2	...	
		1.9	5.6	6.2	3.5	...	U2 genes
		10.3	17.2	11.5	8.9	...	
		3.2	2.3	10.9	3.7	...	
		⋮	⋮	⋮	⋮	⋮	

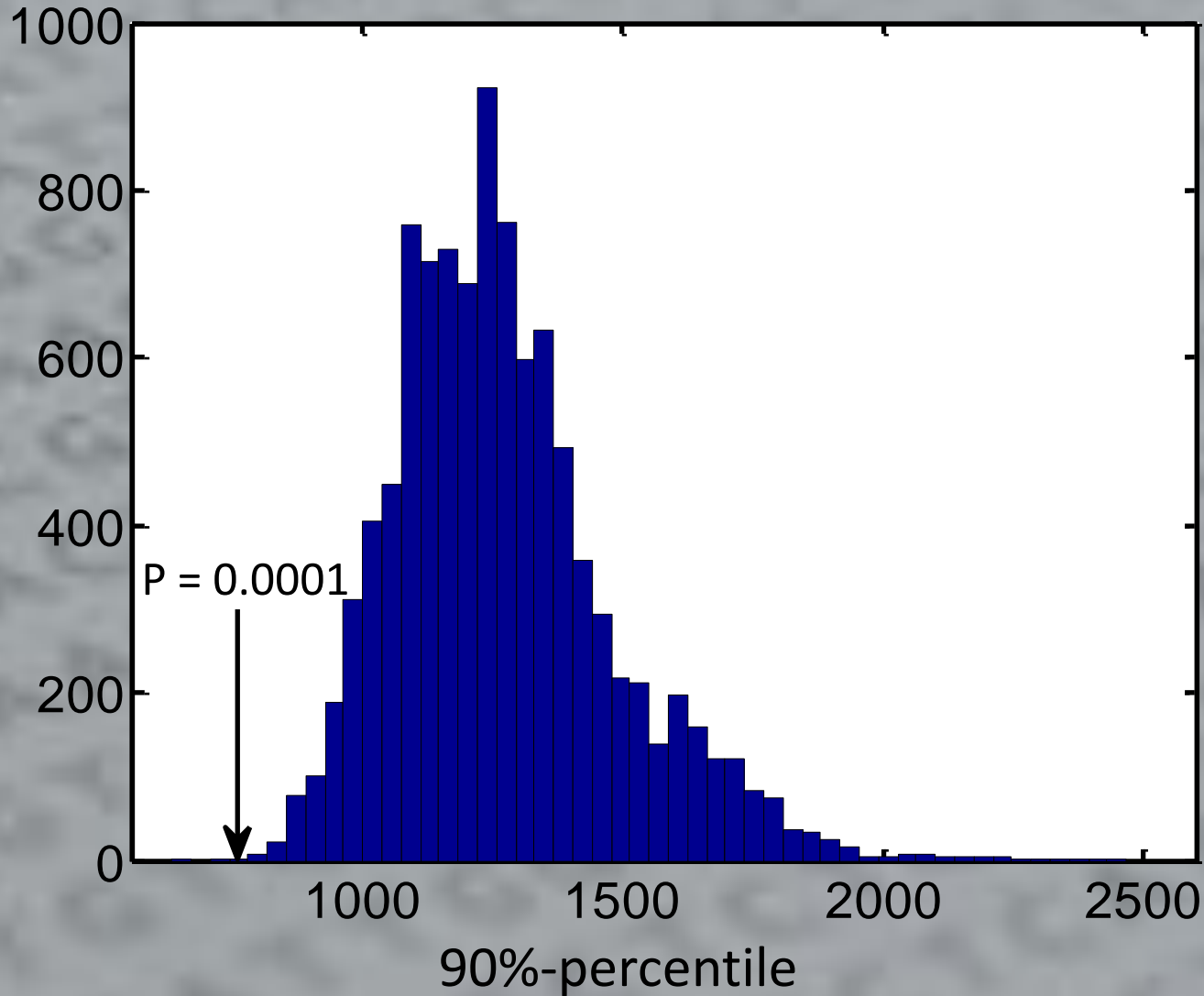
Comparing the distributions



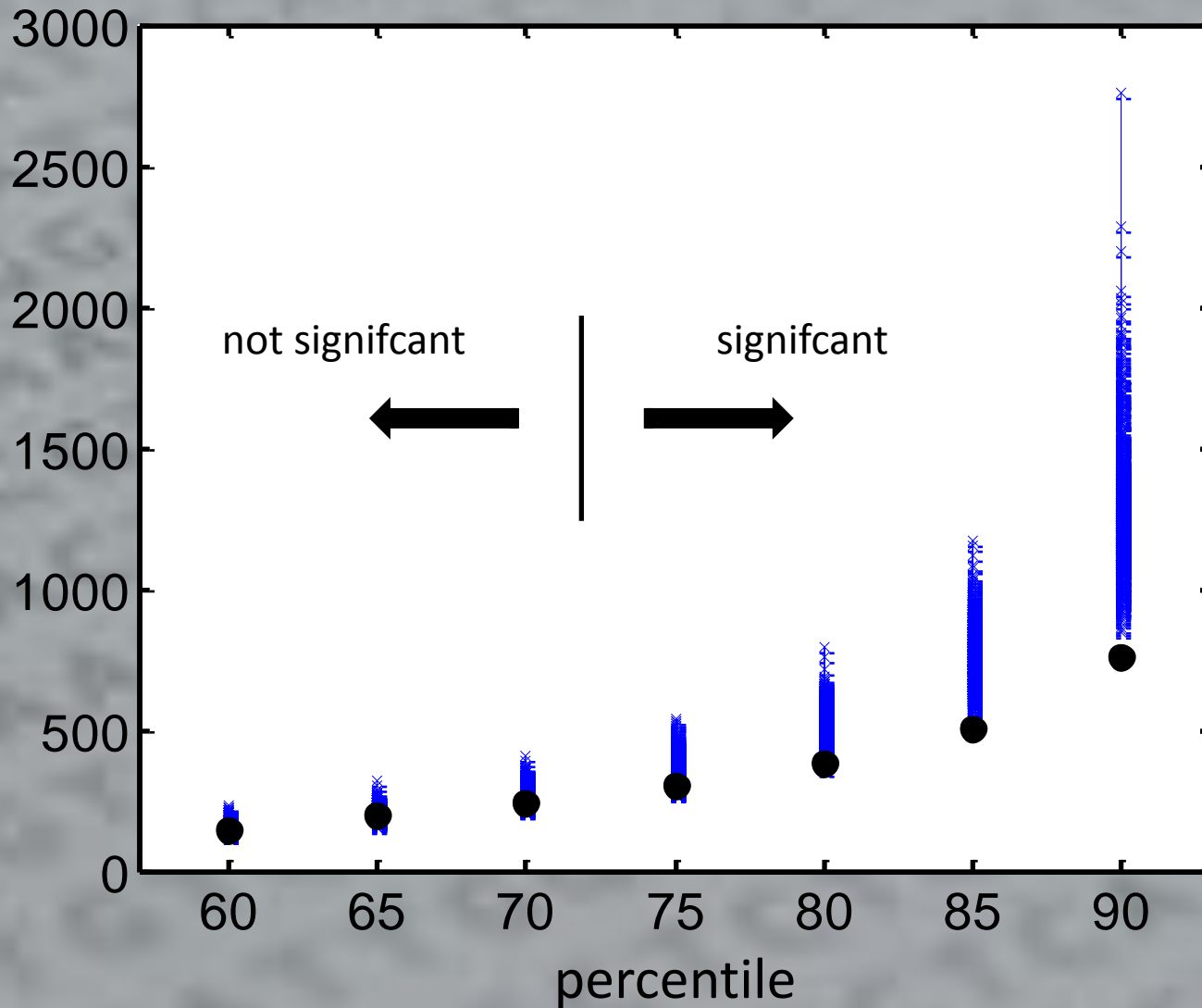
Comparing the distributions



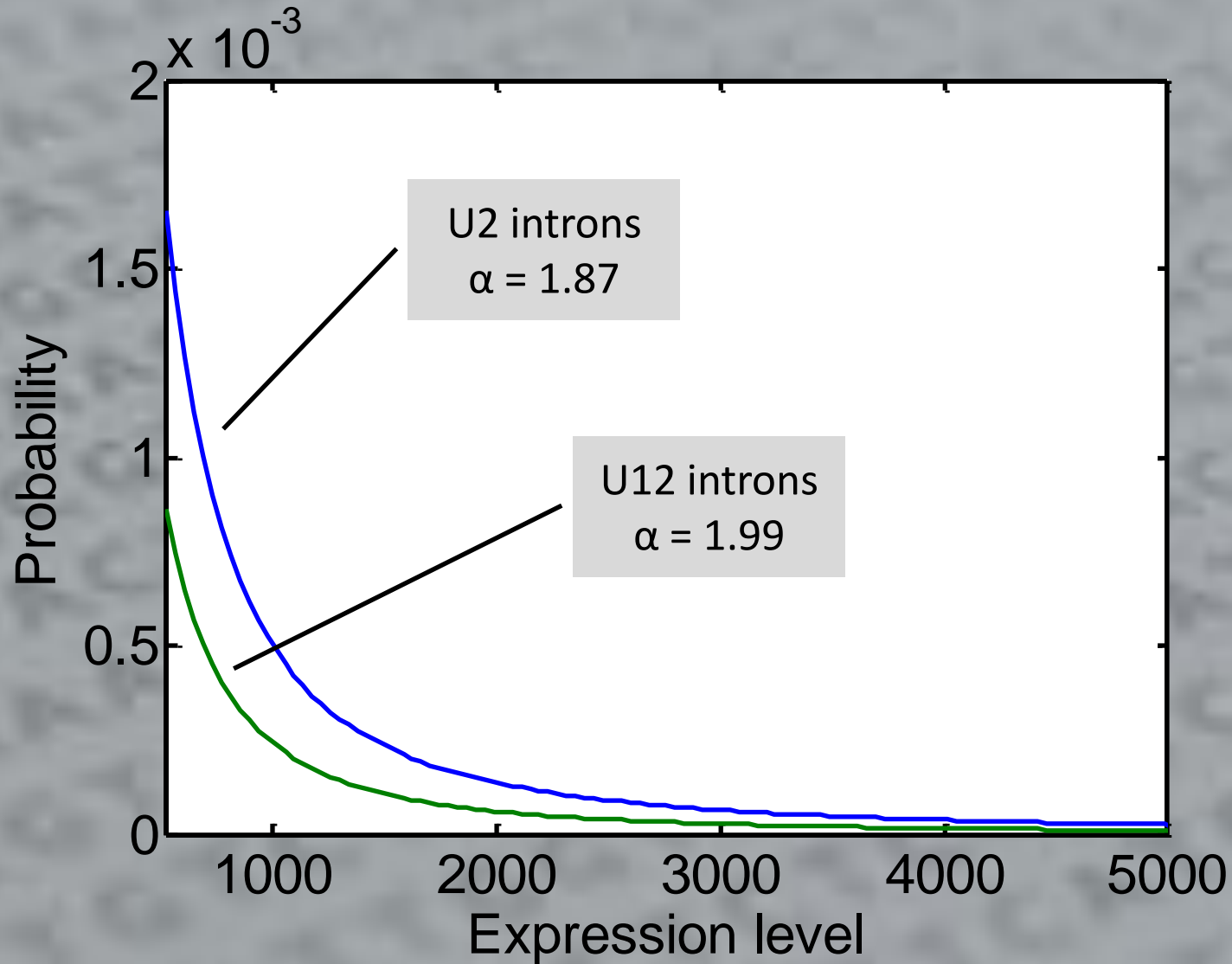
Comparing the tails



Comparing the tails



Power law distribution



Genes that host U12 introns are
depleted of highly expressed
genes

Acknowledgements

Lotem Guy

