

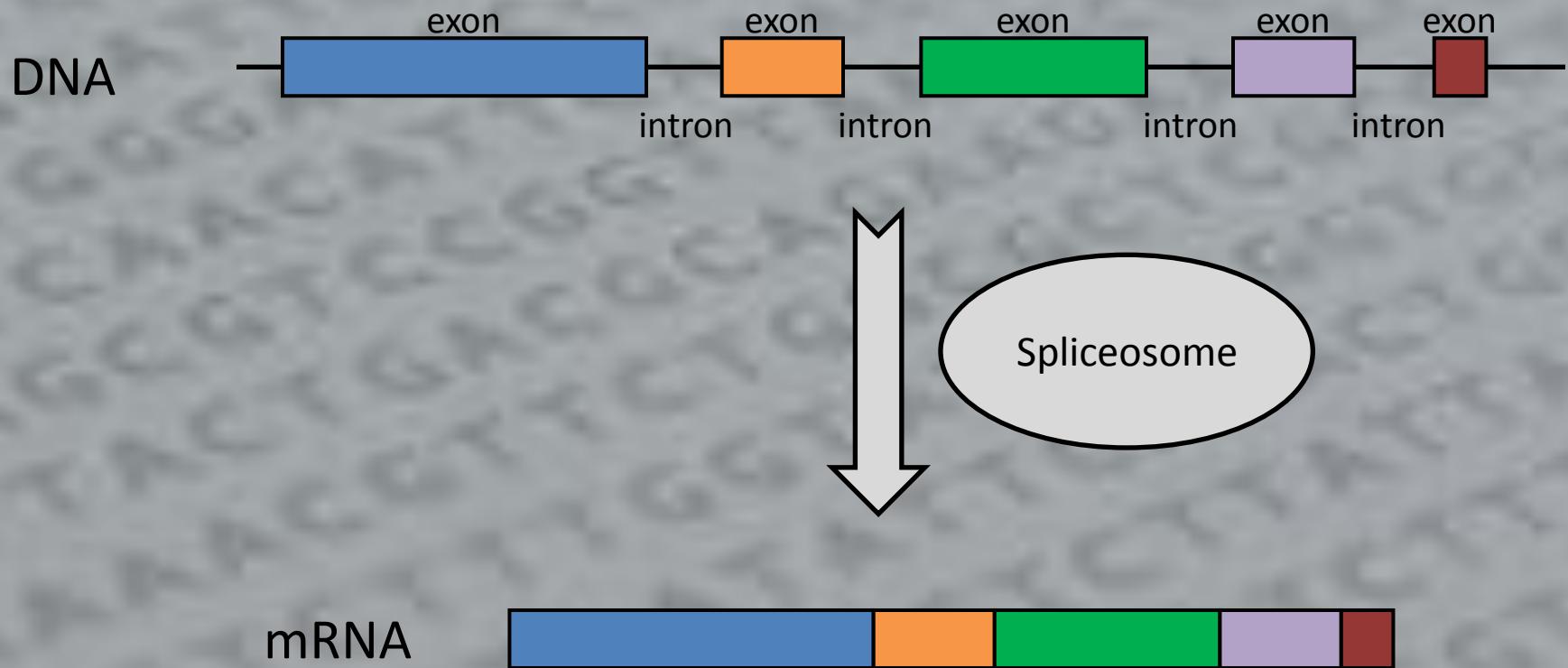
Traces of primordial eukaryotic mechanisms: the regulatory roles of the minor spliceosome

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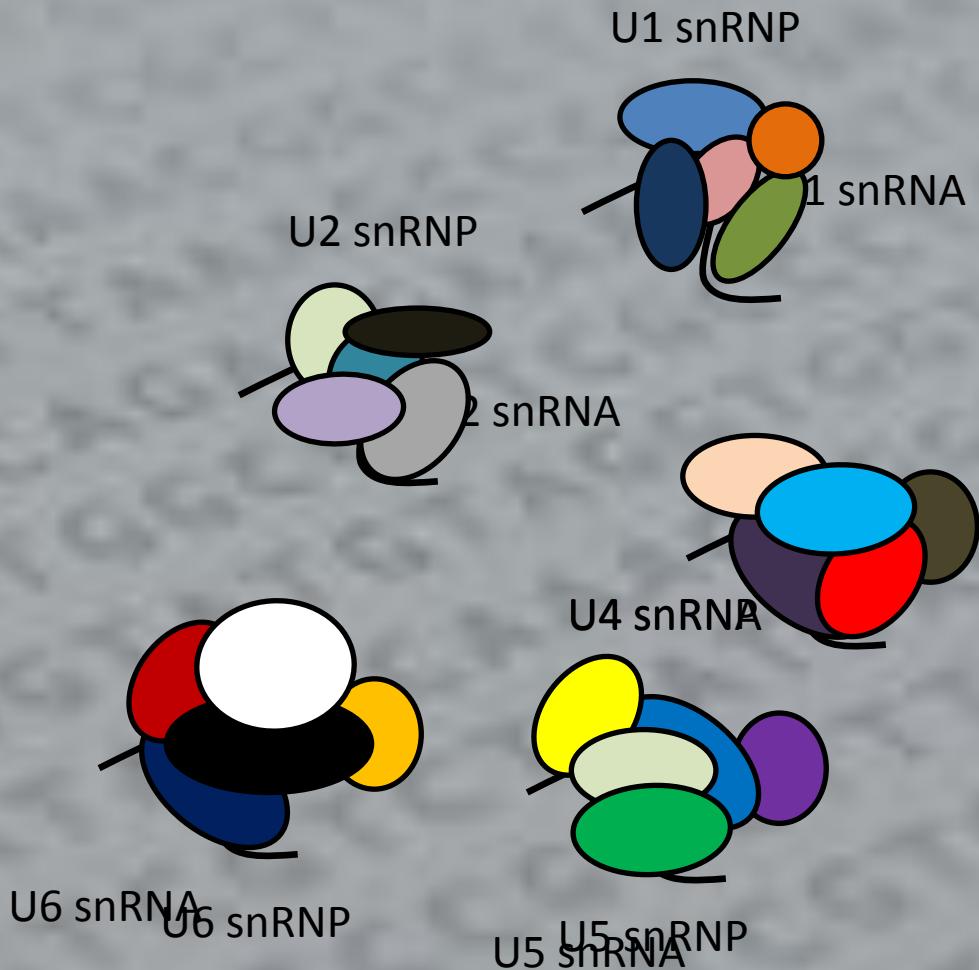
The Hebrew University of Jerusalem

Genes in pieces: the eukaryotic genomic organization

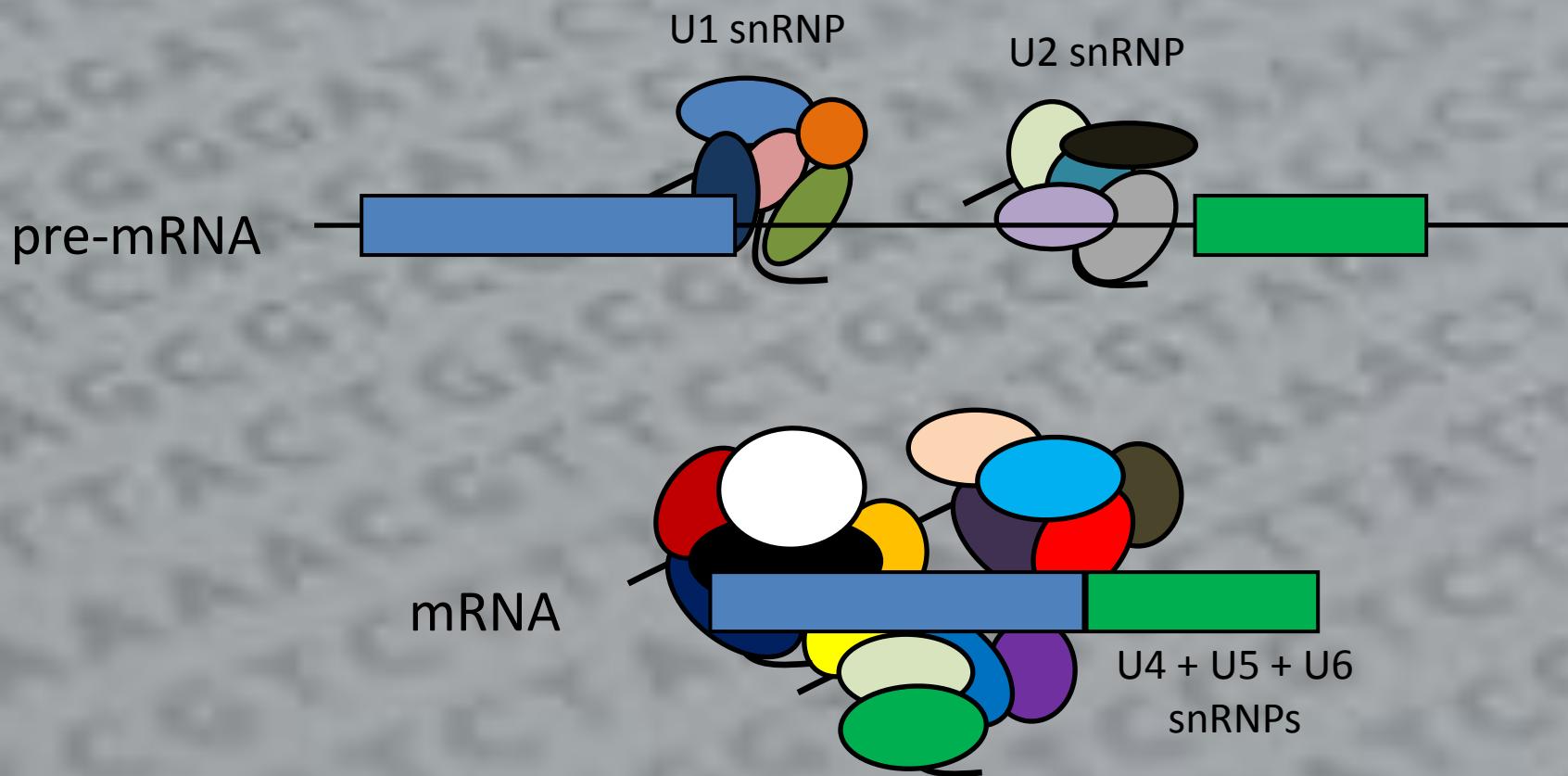


The spliceosome

- 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

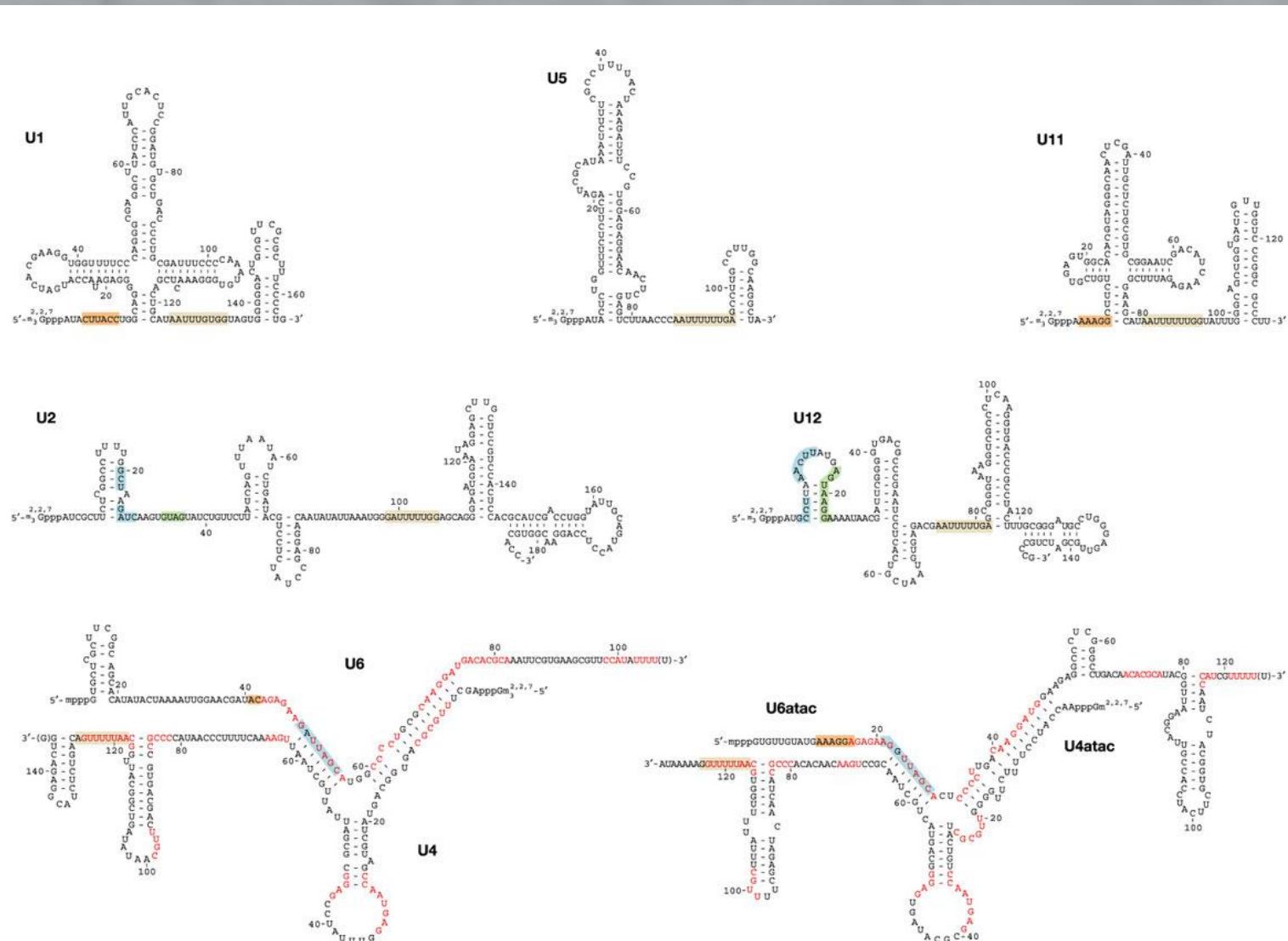


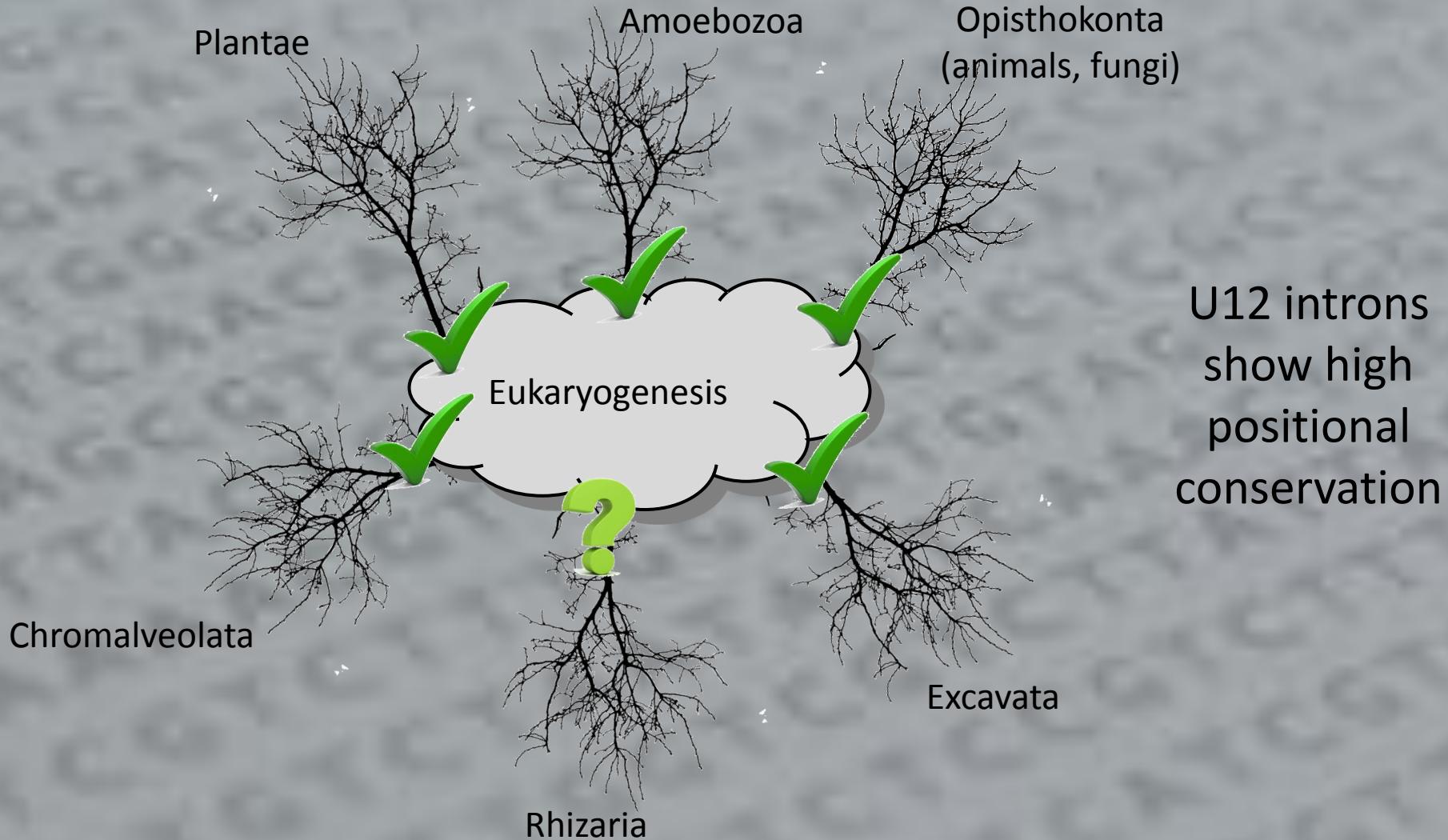
Figure taken from: A.A. Patel & J.A. Steitz (2003). Splicing double: insights from the second spliceosome. *Nature Reviews Molecular Cell Biology* 4, 960-970.

The abundance of the minor spliceosome

	Total	GT-AG	AT-AC
<i>Homo sapiens</i>	695	487	208
<i>Pan troglodytes</i>	524	368	156
<i>Macaca mulatta</i>	479	345	134
<i>Mus musculus</i>	555	394	161
<i>Rattus norvegicus</i>	524	368	156
<i>Canis familiaris</i>	558	394	164
<i>Bos taurus</i>	496	343	153
<i>Monodelphis domestica</i>	478	339	139
<i>Gallus gallus</i>	399	286	113
<i>Xenopus tropicalis</i>	329	234	95
<i>Danio rerio</i>	298	220	78
<i>Takifugu rubripes</i>	337	252	85
<i>Tetraodon nigroviridis</i>	309	232	77
<i>Ciona intestinalis</i>	116	75	41
<i>Drosophila melanogaster</i>	16	7	9
<i>Anopheles gambiae</i>	4	4	0
<i>Apis mellifera</i>	34	31	3
<i>Caenorhabditis elegans</i>	0	0	0
<i>Saccharomyces cerevisiae</i>	0	0	0
<i>Arabidopsis thaliana</i>	246	186	60
	6397	4565	1832

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



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

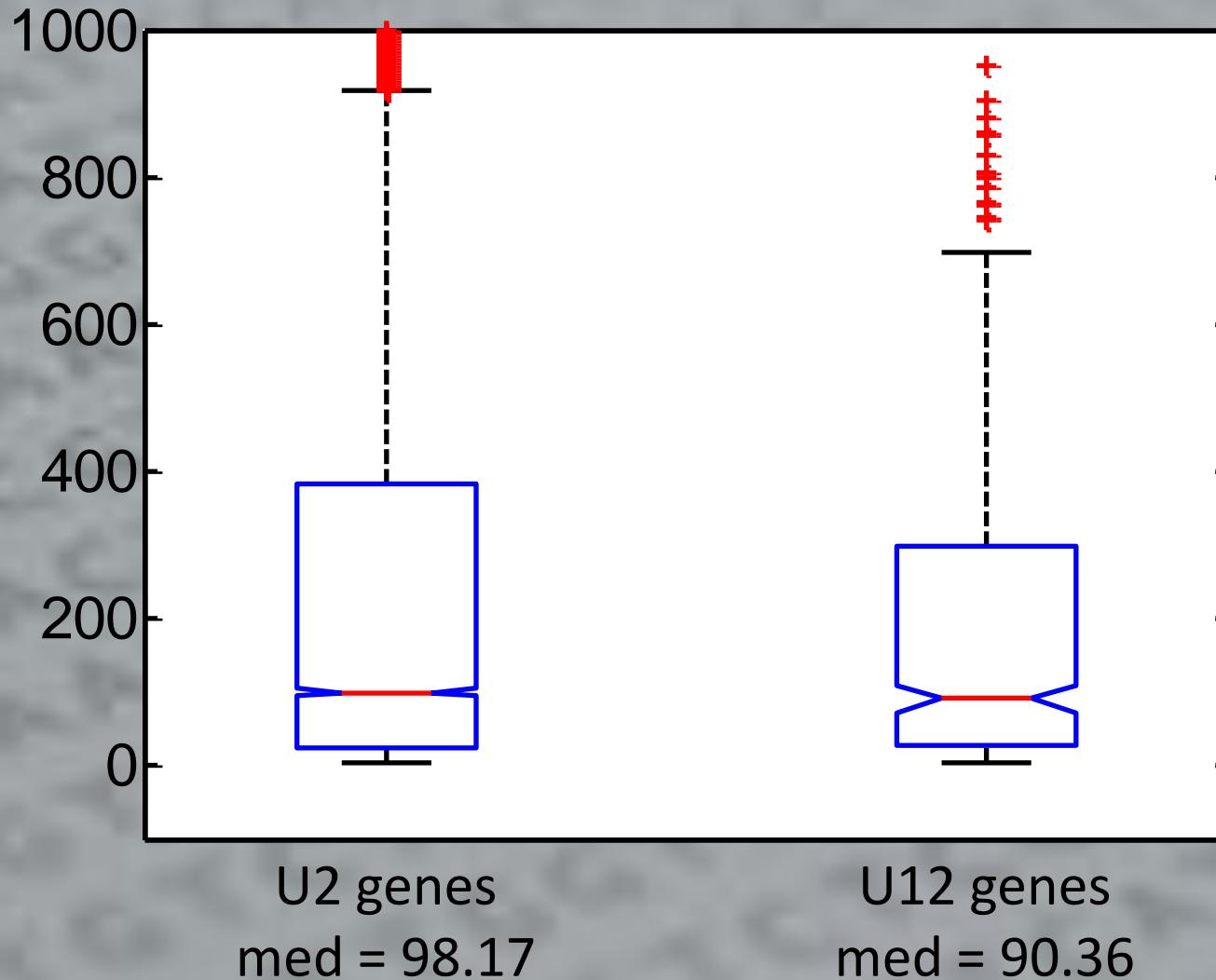
- Grouping human genes
 - U12 genes: have at least a single U12 intron
 - U2 genes: have introns, but none is U12
- Comparing the expression levels of the two groups

Data analysis

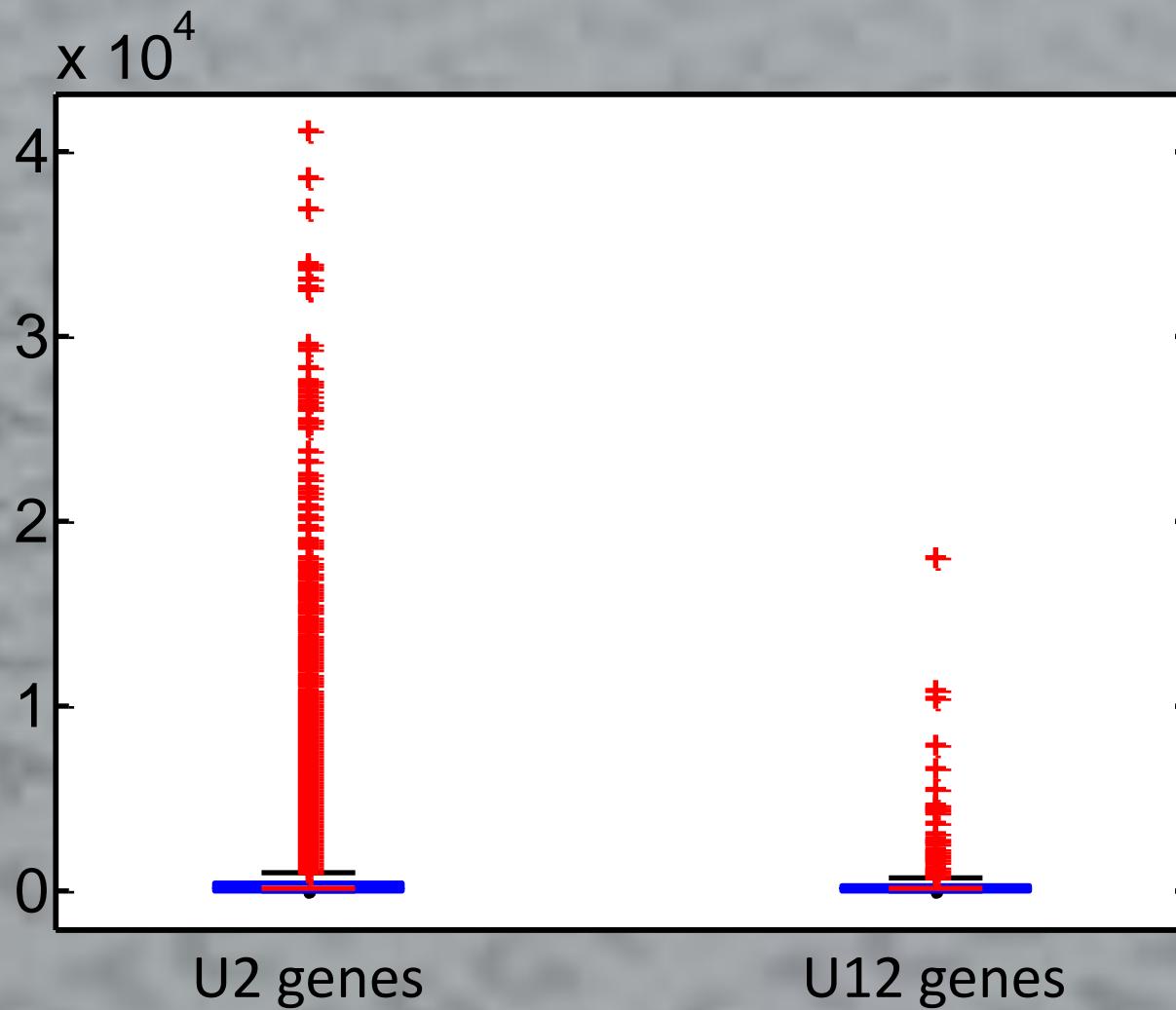
- Microarray expression measurements
 - 32 different tissues
 - 12,502 human genes
 - 503 U12 genes
 - 11,999 U2 genes

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

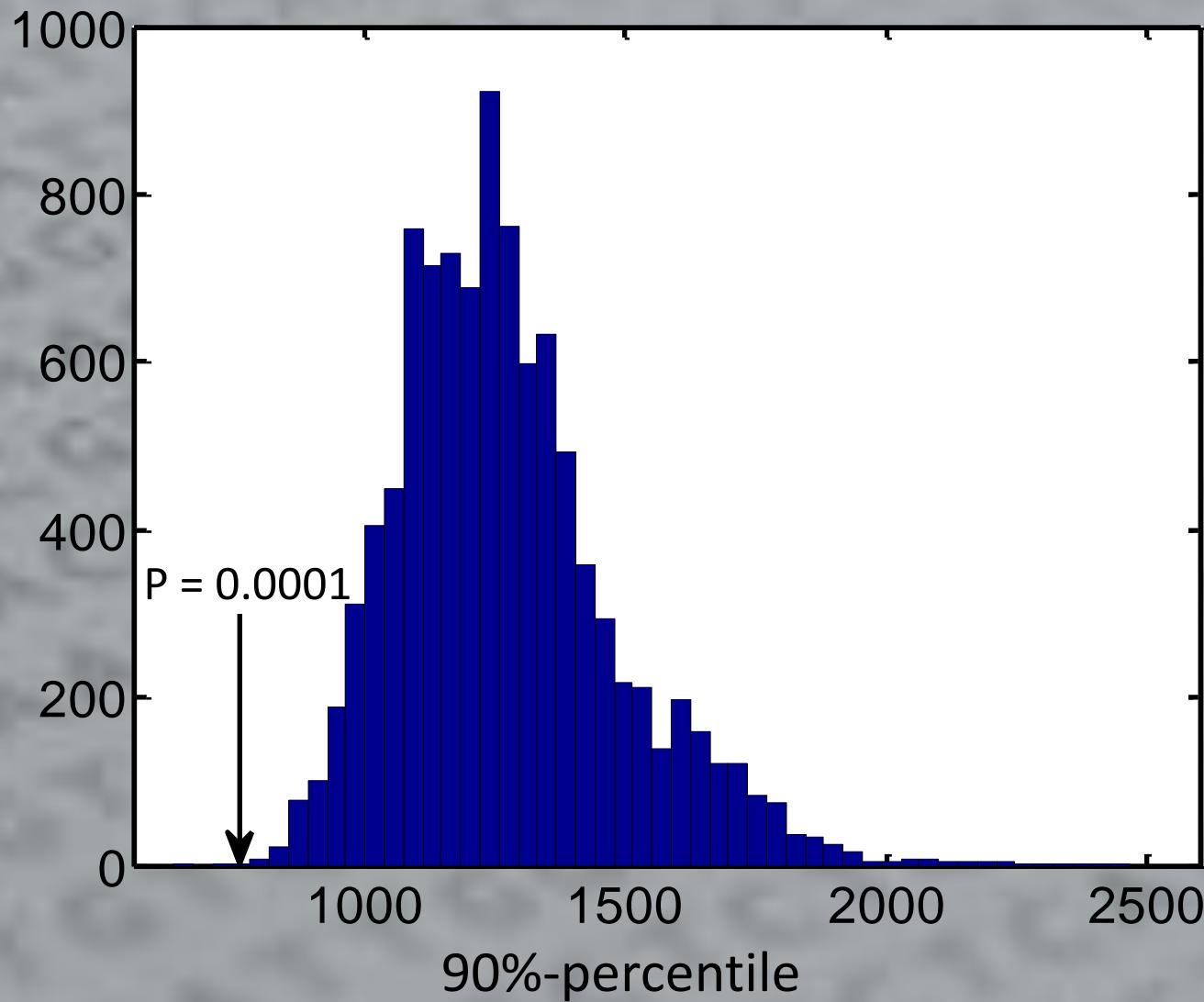
Comparing the distributions



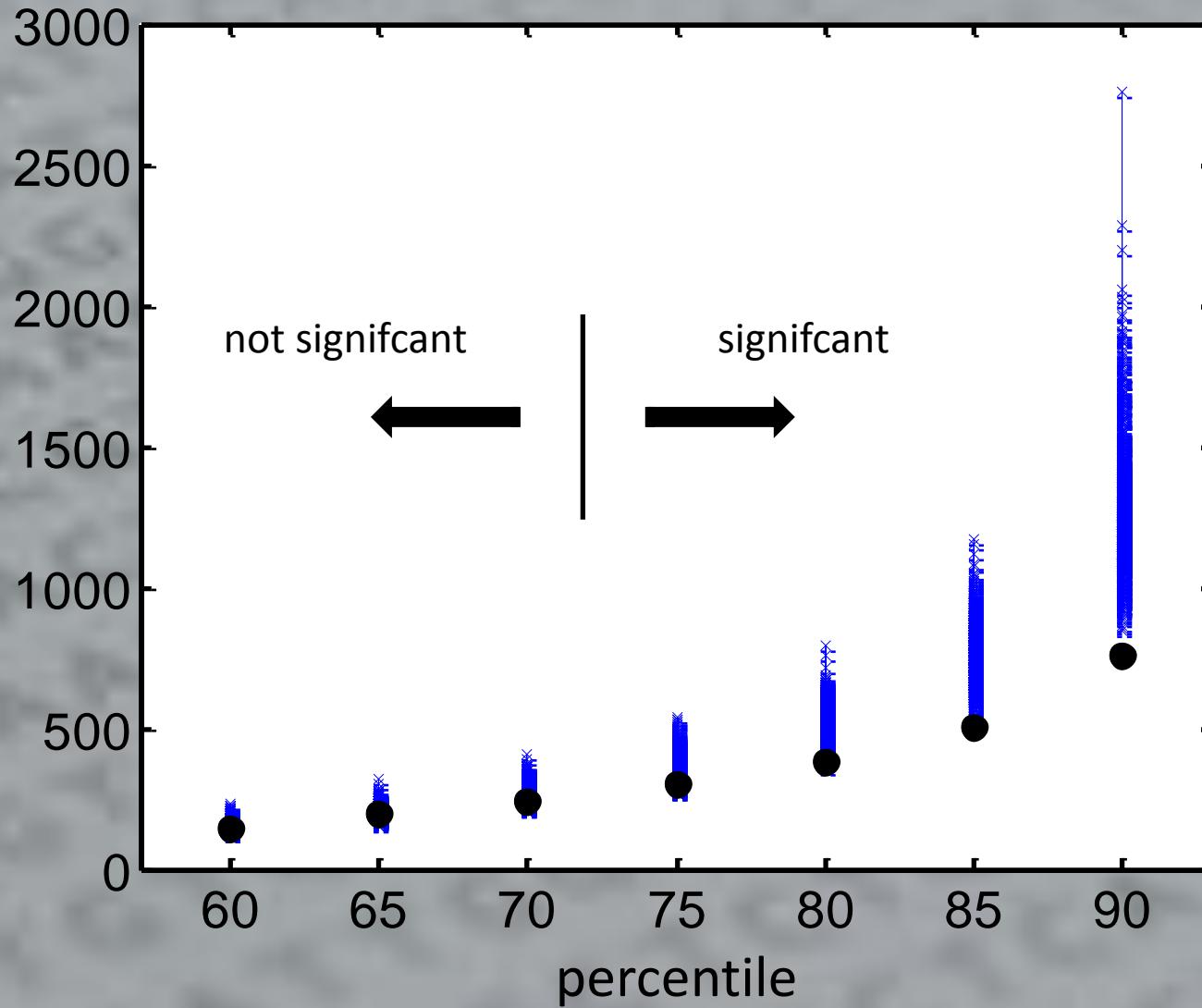
Comparing the distributions



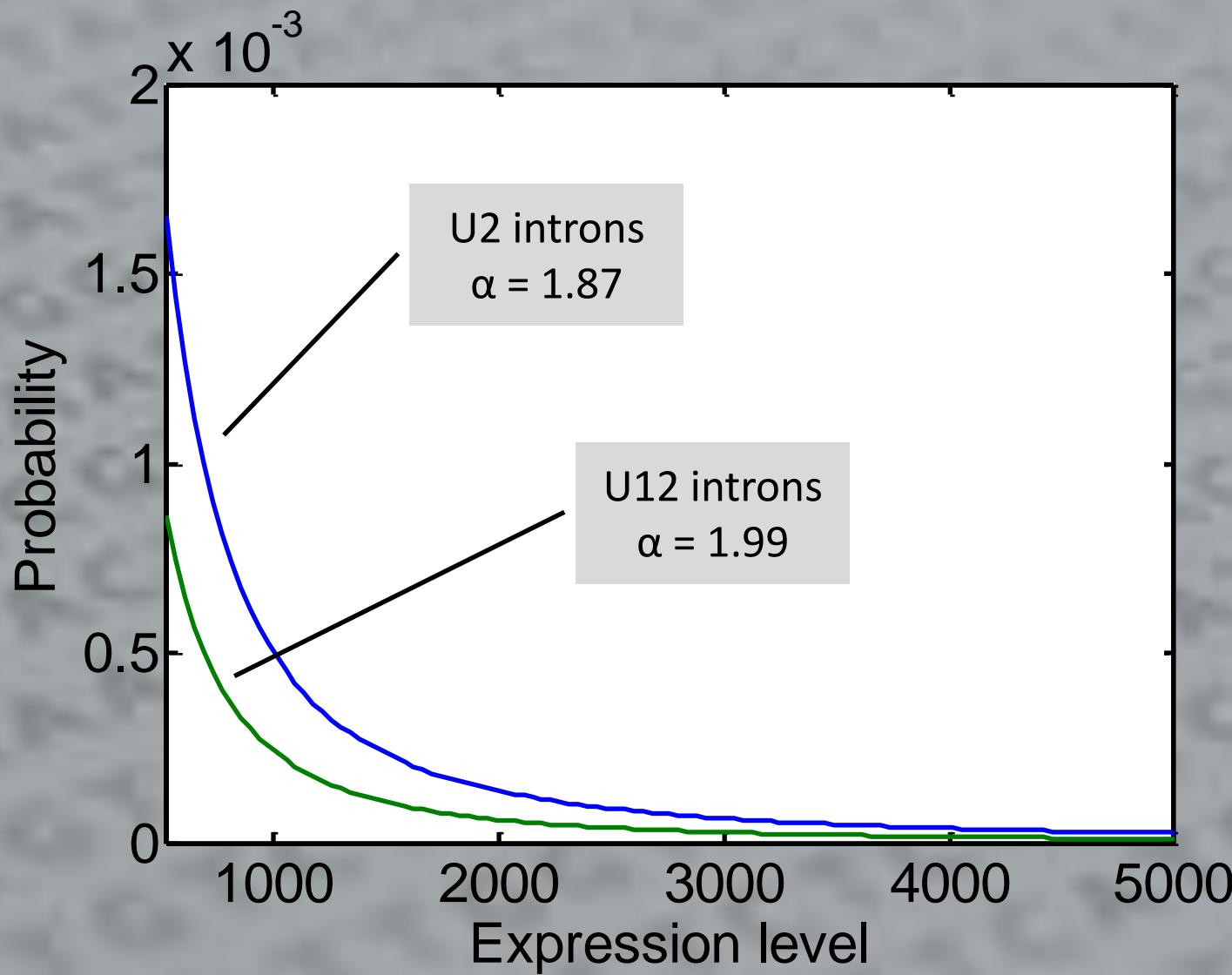
Comparing the tails



Comparing the tails



Power law distribution



Genes that host U12 introns are
depleted of highly expressed
genes

Acknowledgements

Lotem Guy

