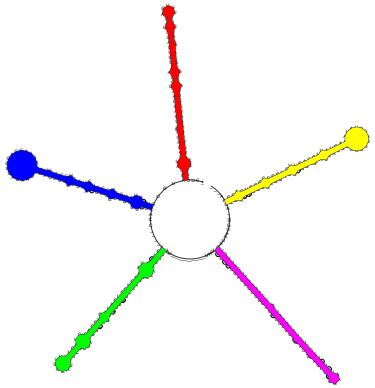
Tales from the microRNA world

Andrea Tanzer



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Bled, February 2004

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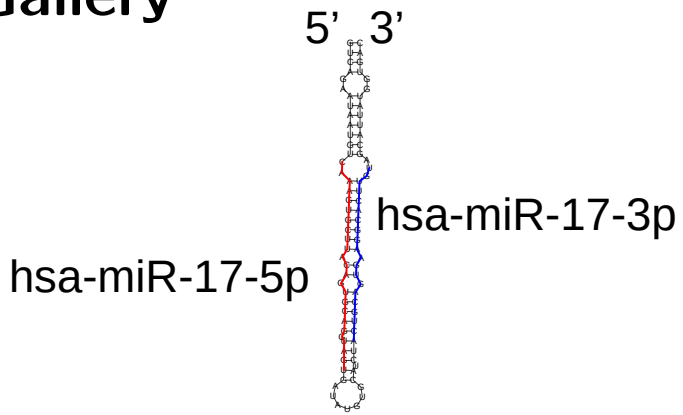
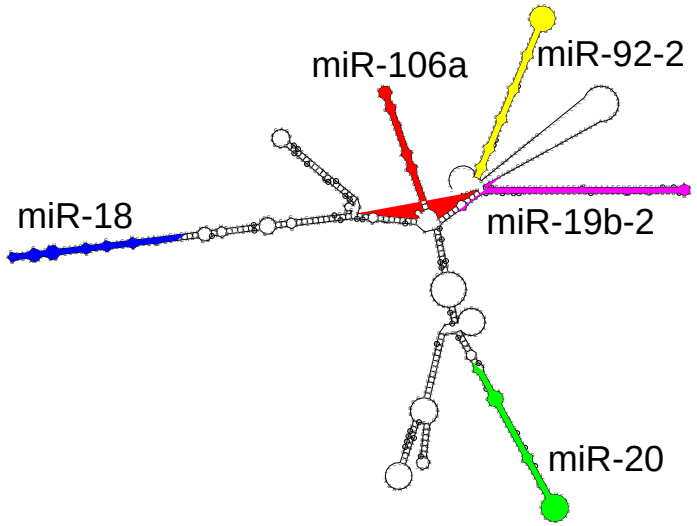
- heterochromatin remodelling

Picture Gallery

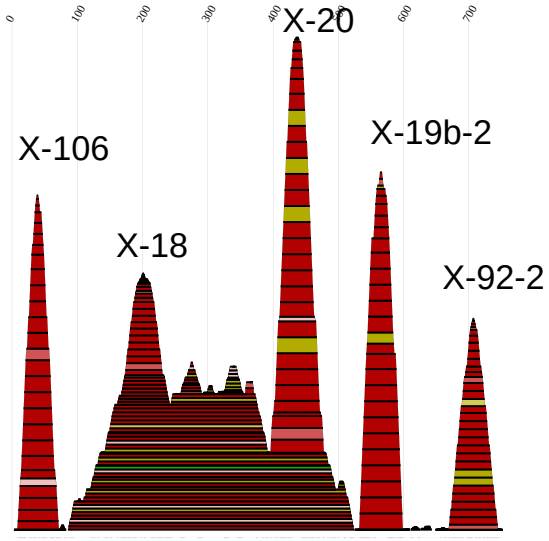
MIR



pri-miRNA

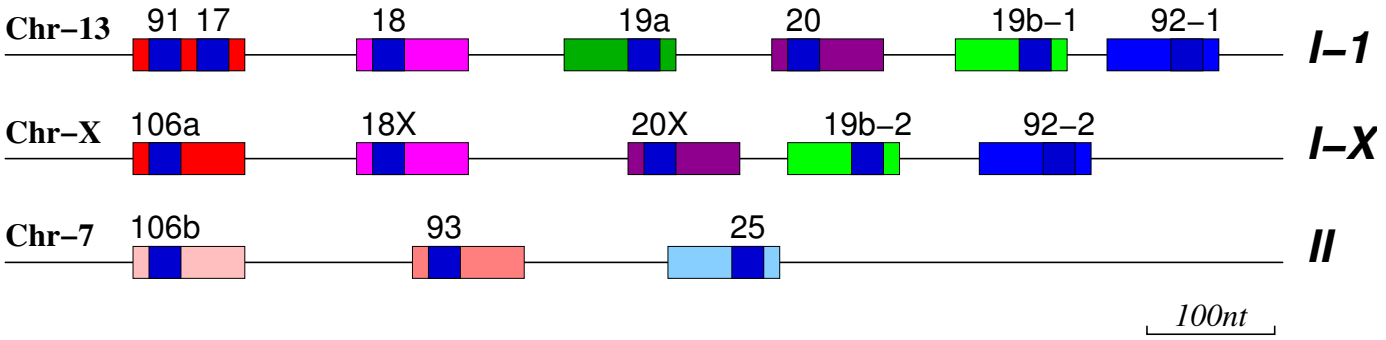


mammalian X cluster



RNAalifold

We are a family:
The mir-17 cluster



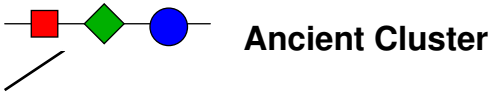
- *H. sapiens* chr. 13: miR-17/18/19a/20/19b/92
- 3 duplicates within human genome (chr.7, 13, X)
- paralogs of miR-17 cluster in

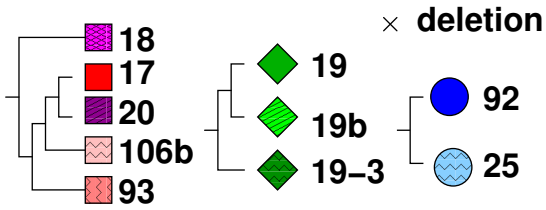
mammalia	3 clusters	mouse, rat, chimp
fish	4 clusters	zebrafish, puffer fish
amphibia	1 cluster	*Xenopus tropicalis*

How could this happen?

Tales from the microRNA world

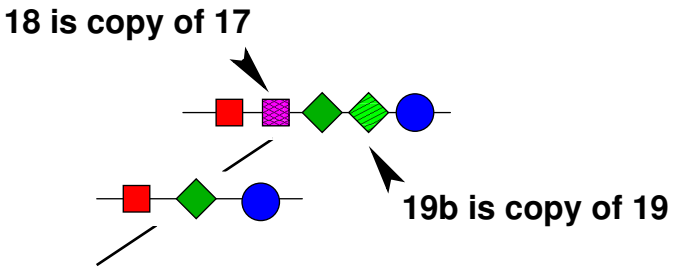
Once upon a time threre was a cute little miR-17 cluster ...

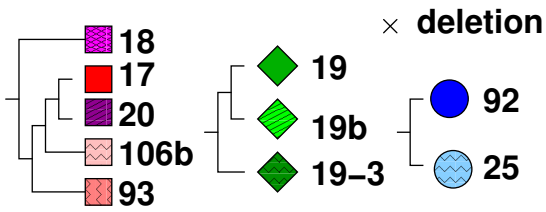




Tales from the microRNA world

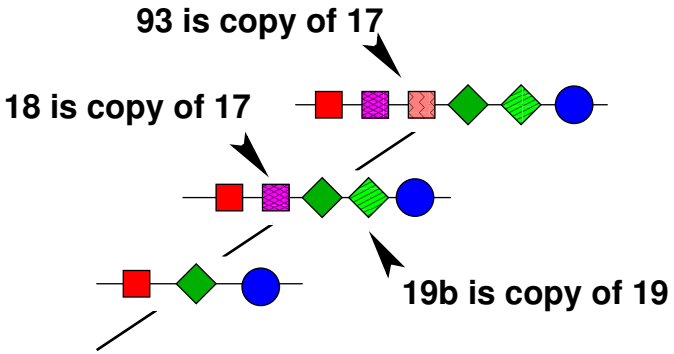
... and one day it started to grow ...

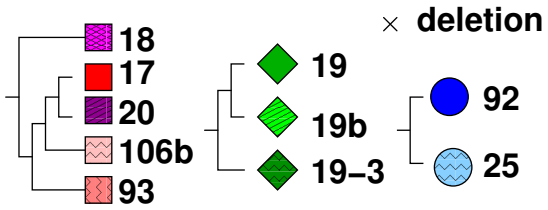




Tales from the microRNA world

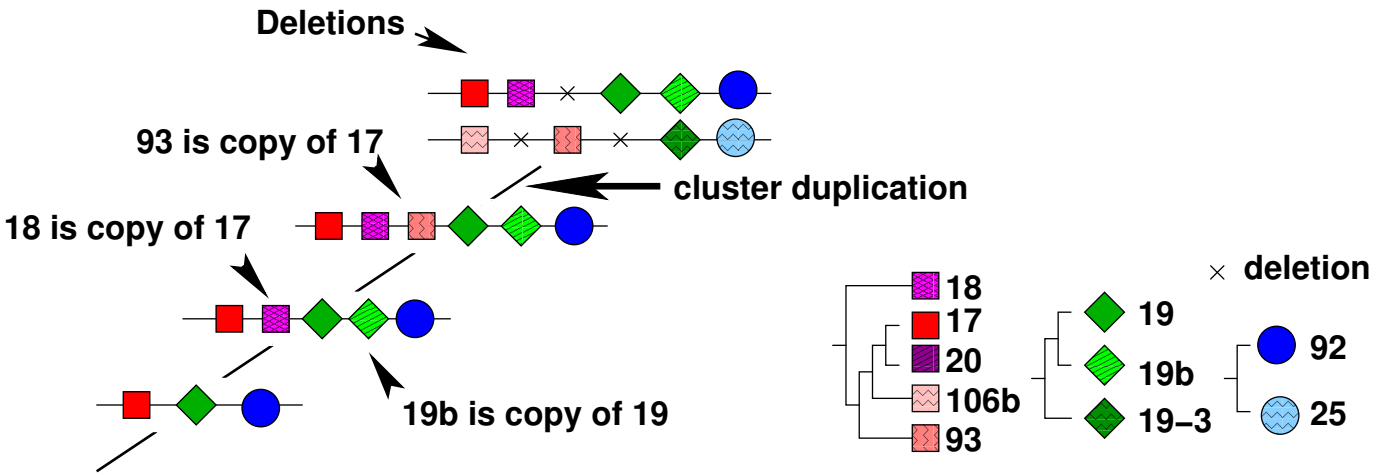
... and it grew bigger and bigger ...





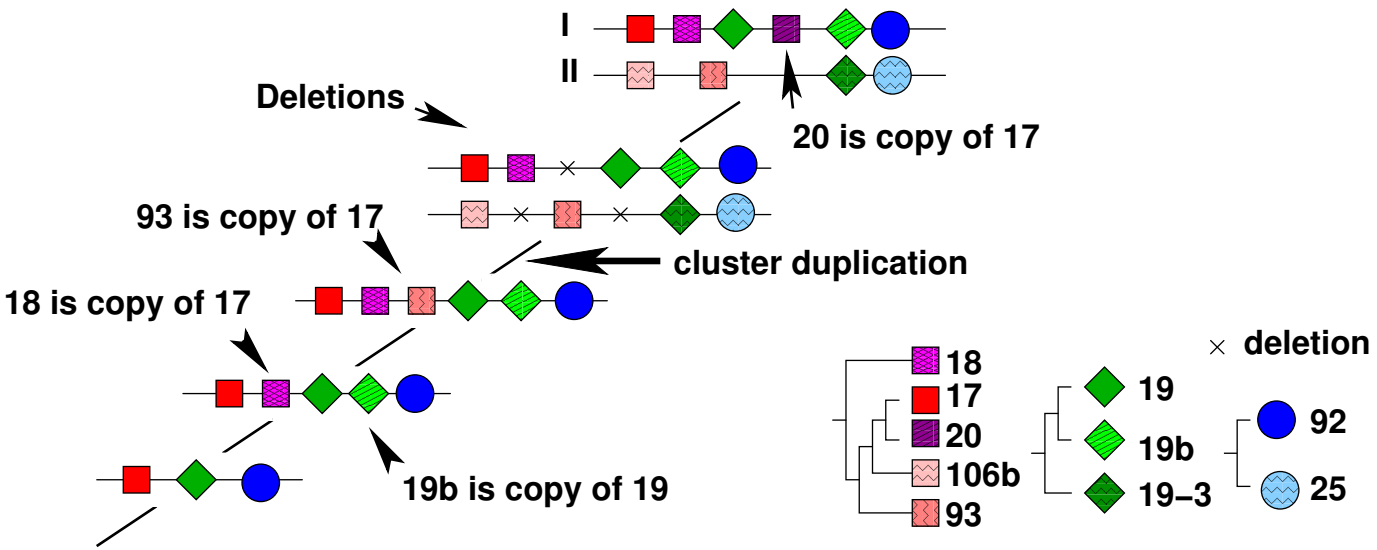
Tales from the microRNA world

... until it was so huge, that it split into
and by this lost some of its parts ...



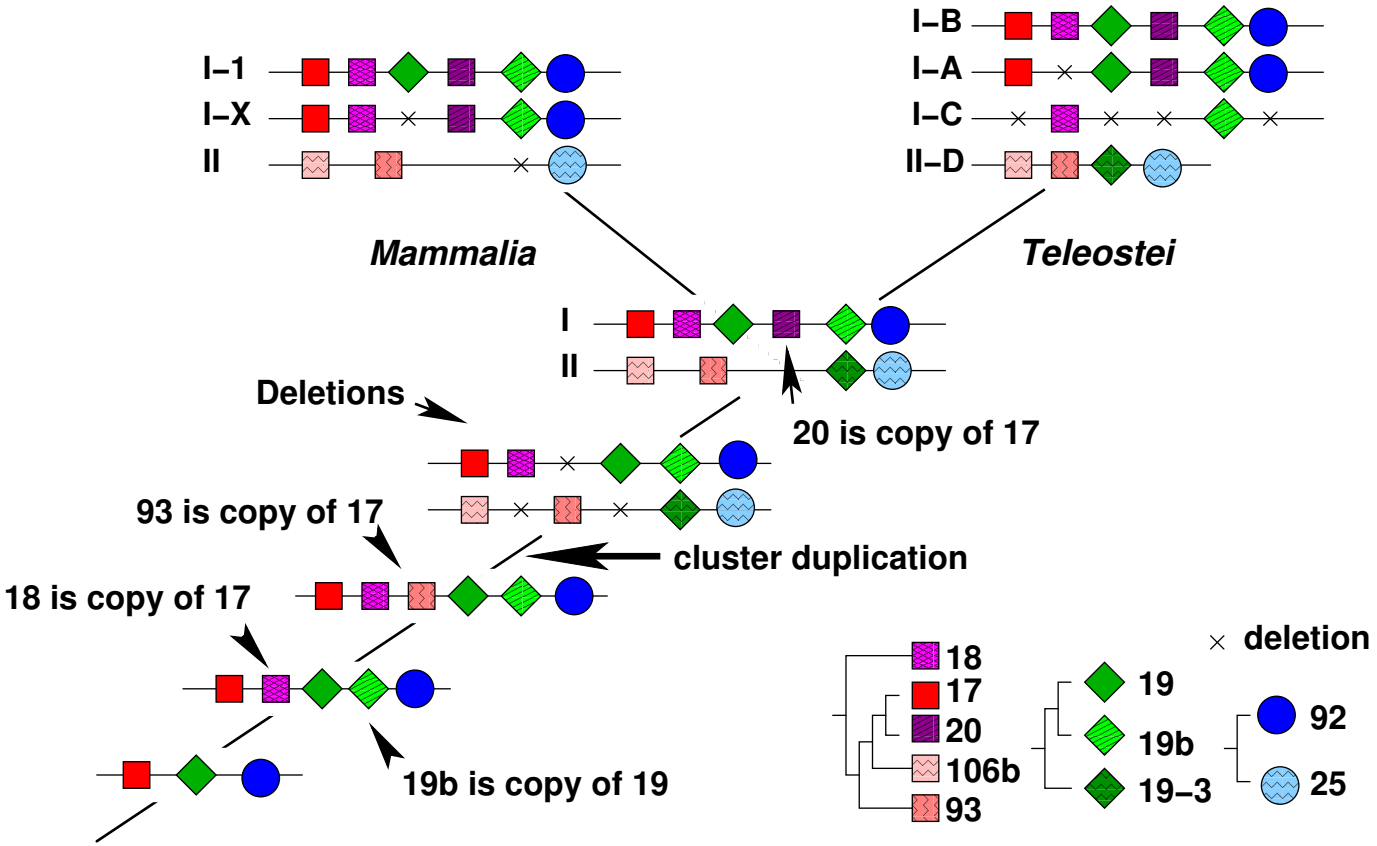
Tales from the microRNA world

... but one of them grew further ...



Tales from the microRNA world

... until they decided to go seperate ways
and they lived happily ever after in the microRNA world.



Toolbox: Standard Procedures

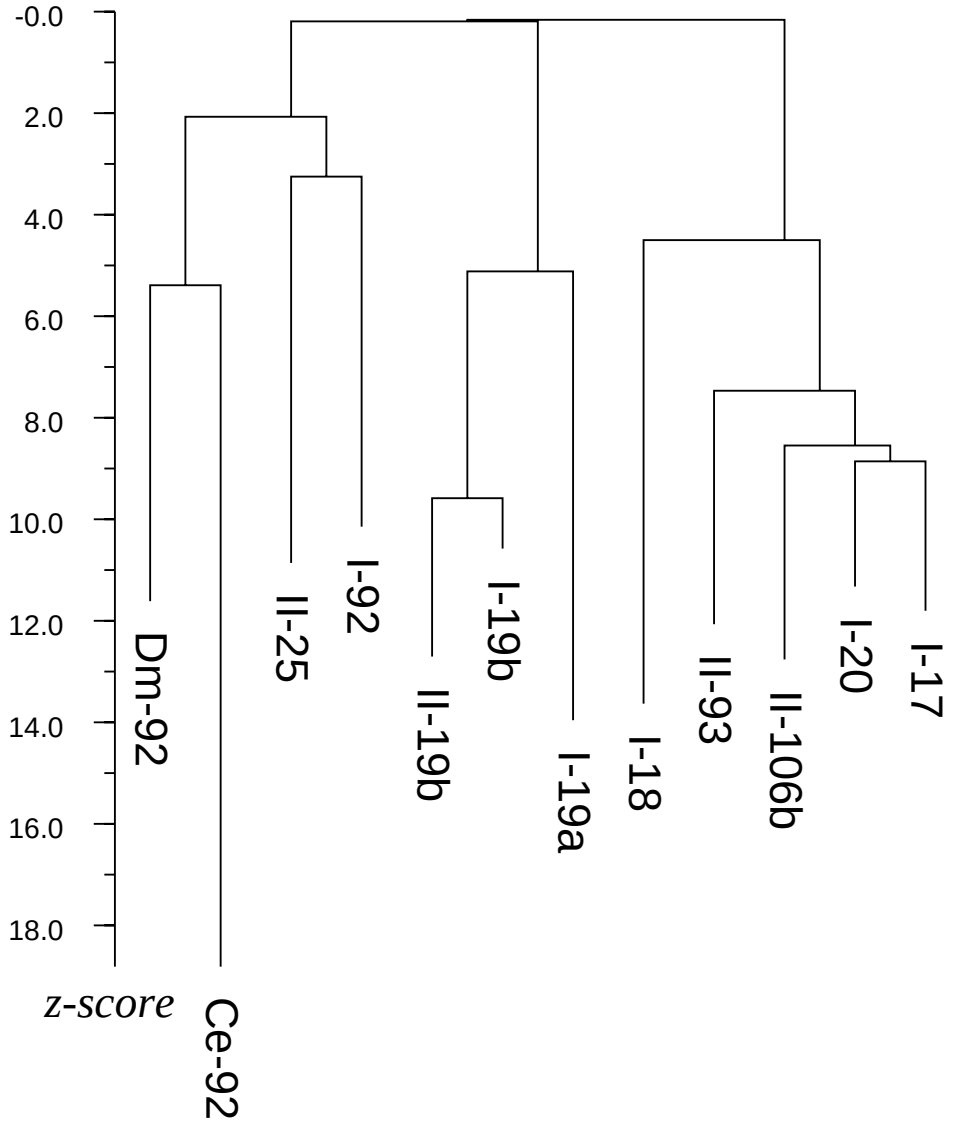
- blastn
- clustalw
- RNAfold (`Vienna RNA Package`)
- RNALfold (`Vienna RNA Package`)
- RNAalifold (`Vienna RNA Package`)
- Maximum Parsimony (`phylip` package)
- Neighbor-joining (`phylip` package)

Toolbox: WPGMA clustering

$$z(I, J) = \frac{s(I, J) - m}{\sqrt{v}} \tag{1}$$

- two pre-miRNAs I and J
- identity score $s(I, J)$ for their pairwise alignment
- random permutation of positions of I and J independently of each other results in sequences I_π and J_π
- mean score m and the variance v are estimated from a sample of 1000 alignments of sequences I_π and J_π
- z-score used as similarity measure of I and J for WPGMA clustering

The WPGMA Tree



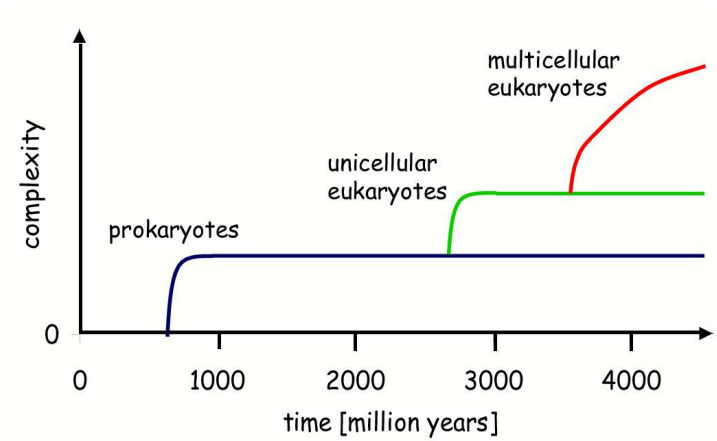
Reconstruction of evolution of mir-17 clusters is based on this tree

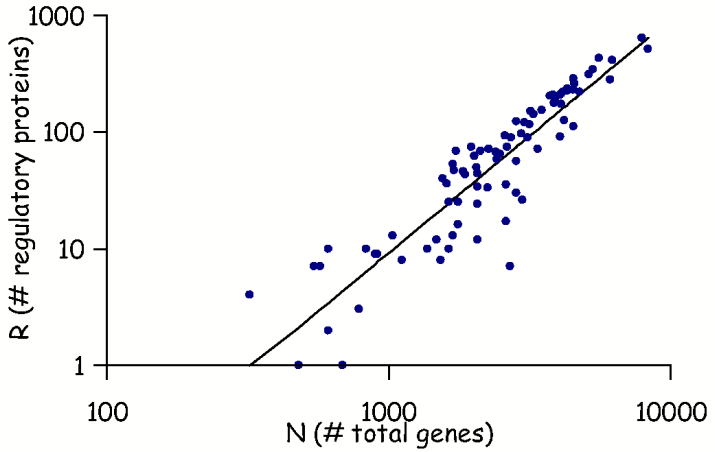
Summary

- miRNAs live in custers
- polycistronic transcripts
- propagation of clusters within genome by duplication
- duplication of miRNAs within a cluster
  in the course of evolution

Conclusion

Problem:





increasing complexity of organisms

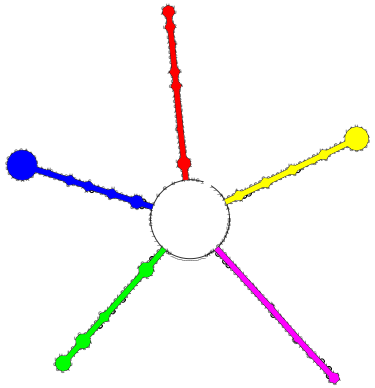
regulatory genes scale quadratic with no. of genes

Conclusion

Solution:

- microRNAs!
- easy to handle in transcriptional regulation
- produced quickly
- act almost immediately
- regulate regulators

Thanx



Transcription rates in Eurkaryotes

Transcription	40 nt/sec
Translation	15 aa/sec
gene of 10.000 nt	
	after
transcription finished	4 min
release and polyadenylation of 3' end	20 min
transport to cytolasm	25 min
translation	more than 4h

Transcription rates in Prokaryotes

Transcription:	40 nt/sec
Translation:	15 aa/sec

mRNA of 5000bp
Protein of 180kD

transcription	2 min.
translation	2.5 min.

transcription and translation occures simultaneously!