

RNA folding during transcription

(Co-transcriptional folding)

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RNA folds into cool tertiary structures

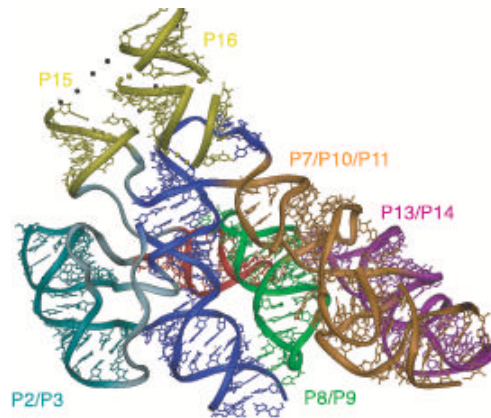
tRNA

~25 KDa



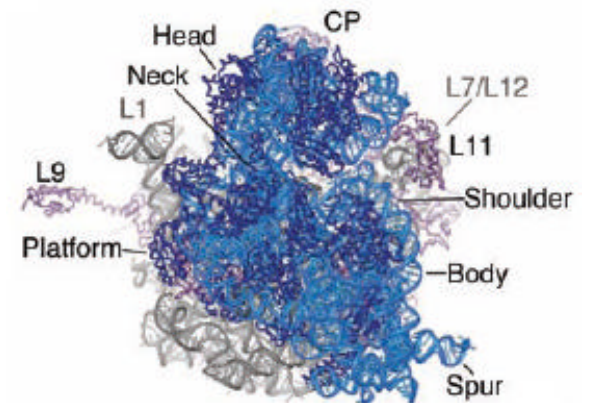
P RNA

~115 KDa



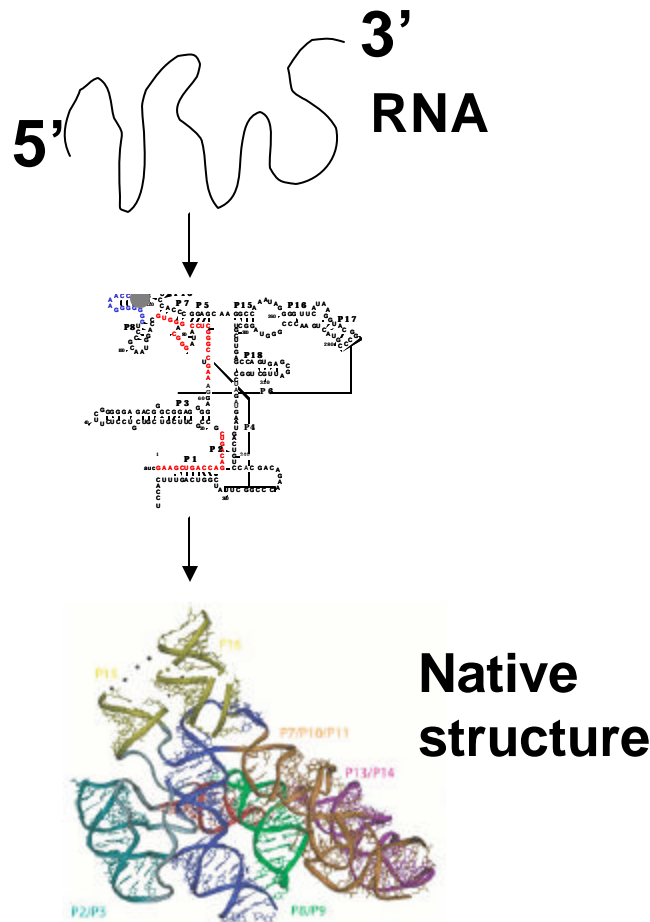
ribosome

> 10³ kDa

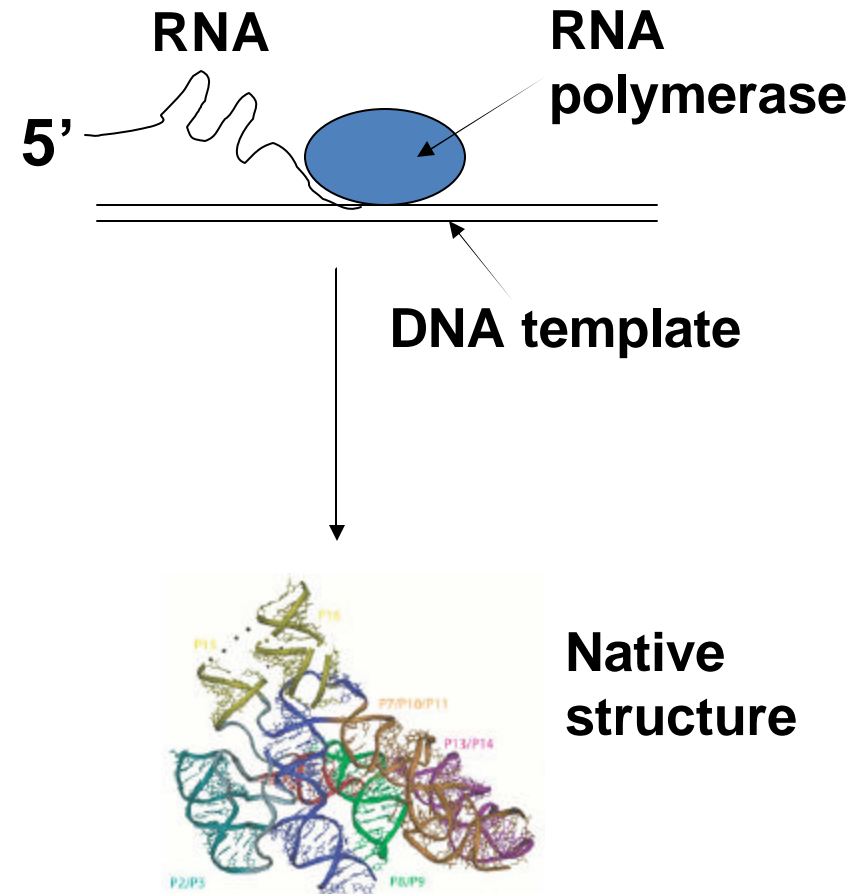


(Biophysics) Mg^{2+} -initiated RNA folding versus (Biology) transcription-initiated RNA folding

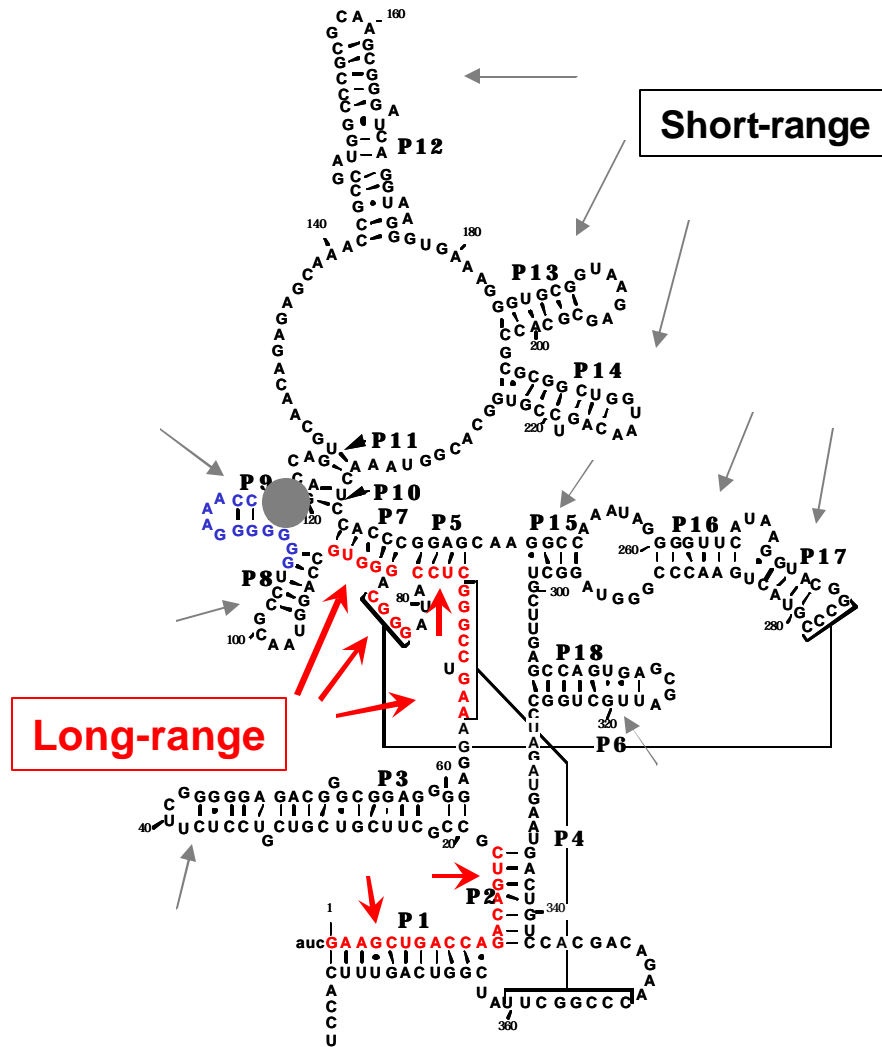
Mg^{2+} -initiated



Transcription-initiated

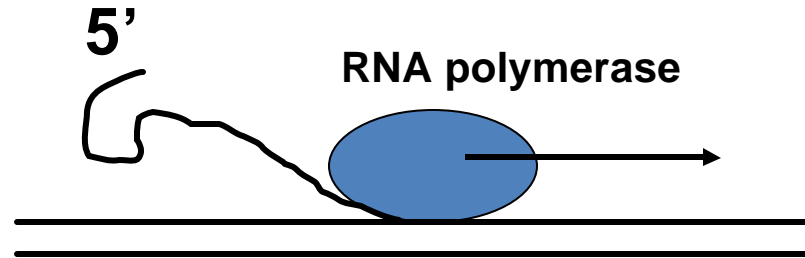


The obvious problem spots: Long-range helices

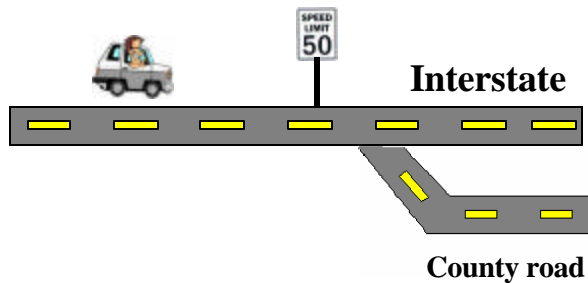


Things that matter in folding during transcription

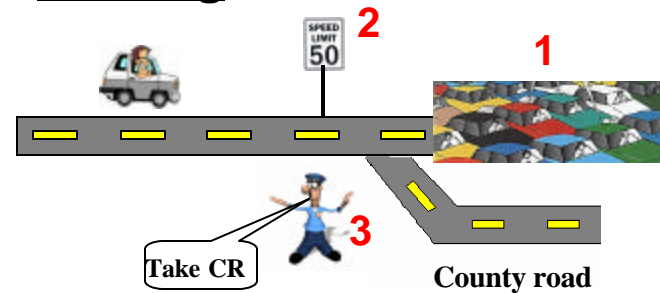
Polarity



Speed



Pausing



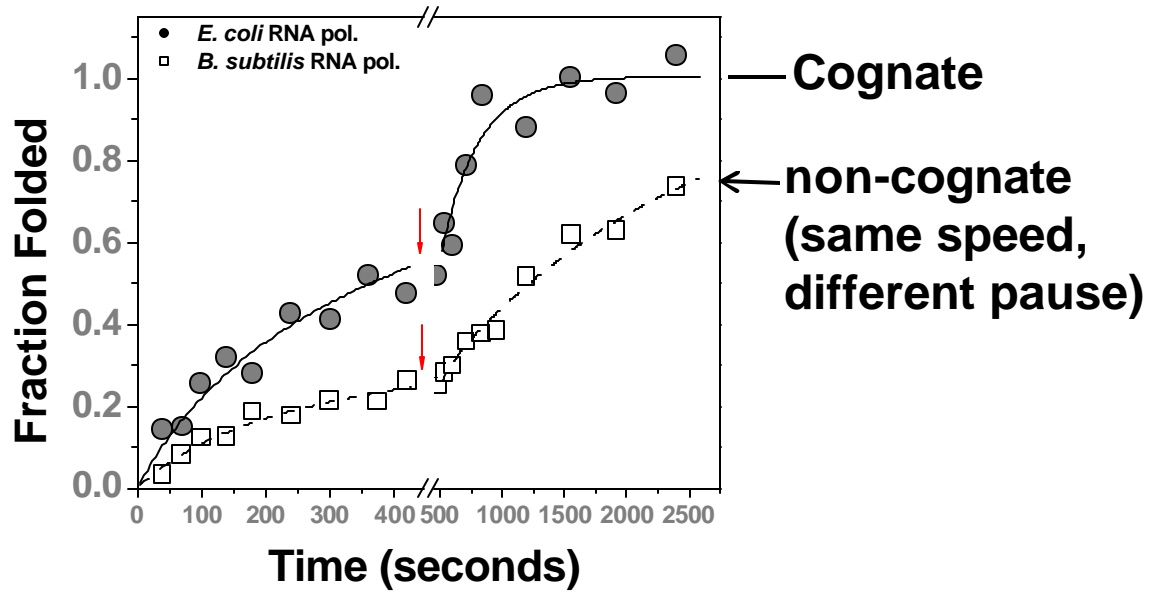
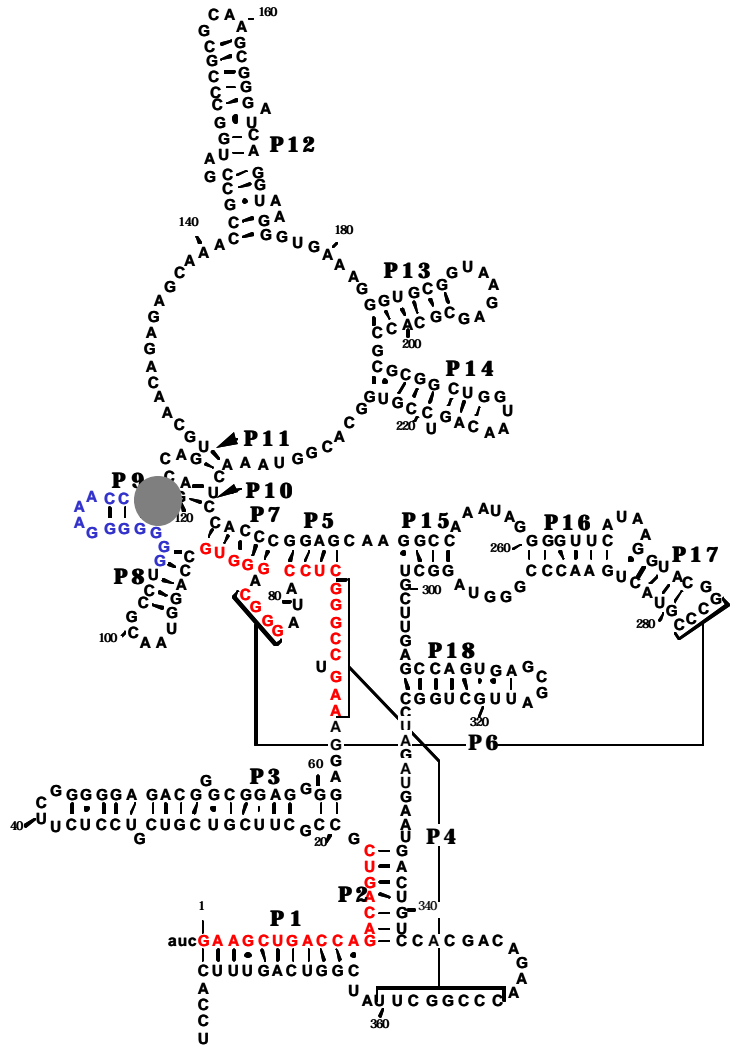
Timing is everything.

(1) Location.

(2) Timing.

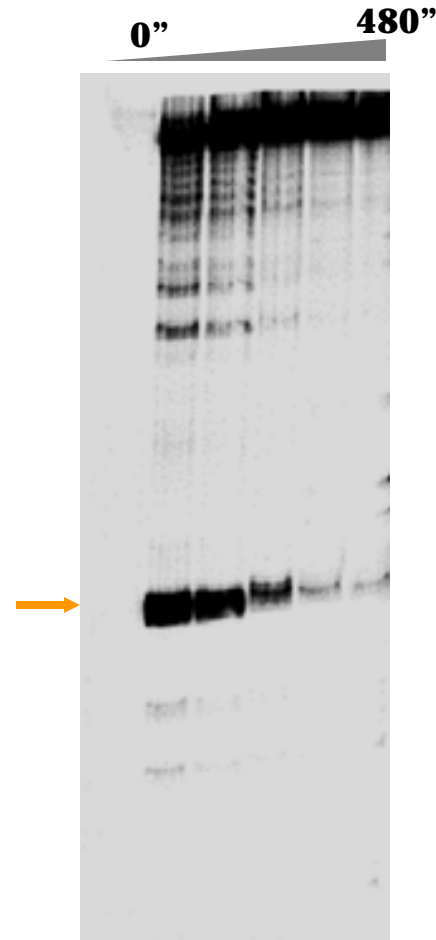
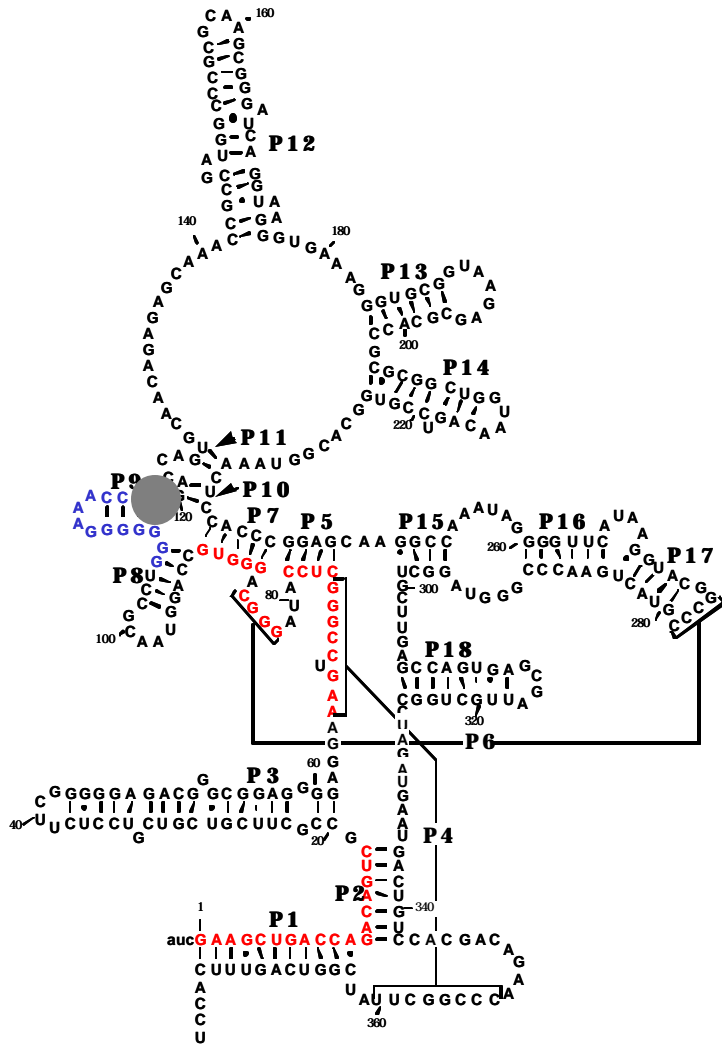
(3) Interaction with RNA polymerase?

Folding of *E. coli* RNase P RNA



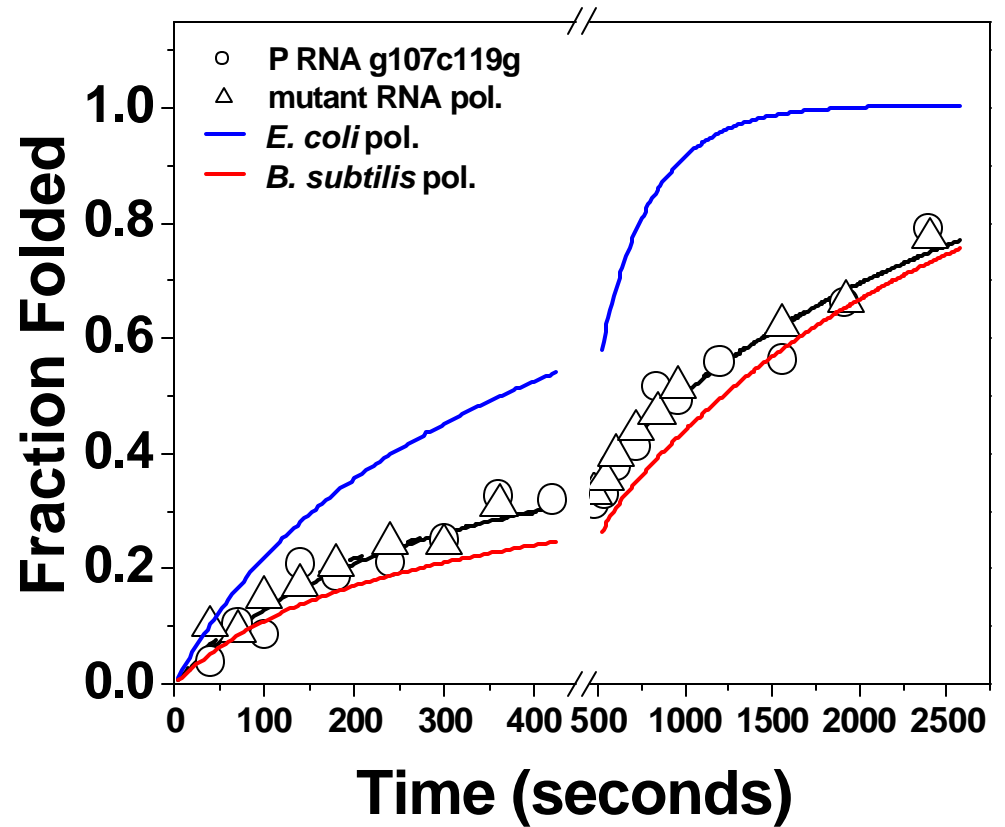
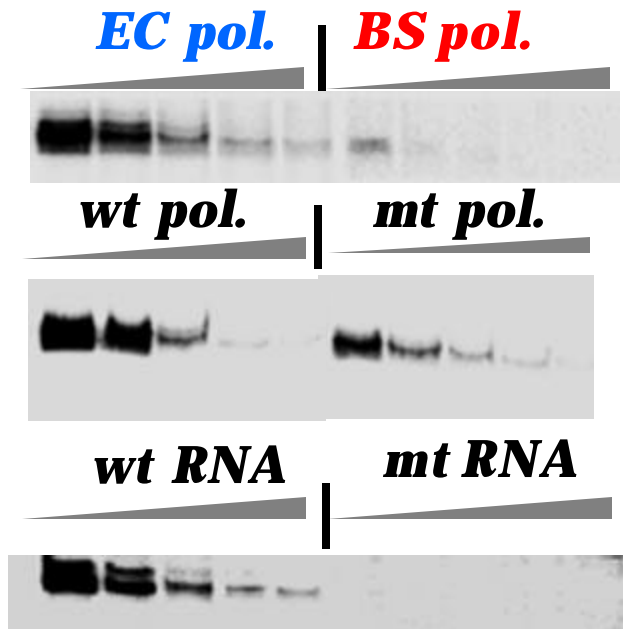
Speed doesn't matter.
Mg²⁺-initiated folding even slower.

Big-time Pausing

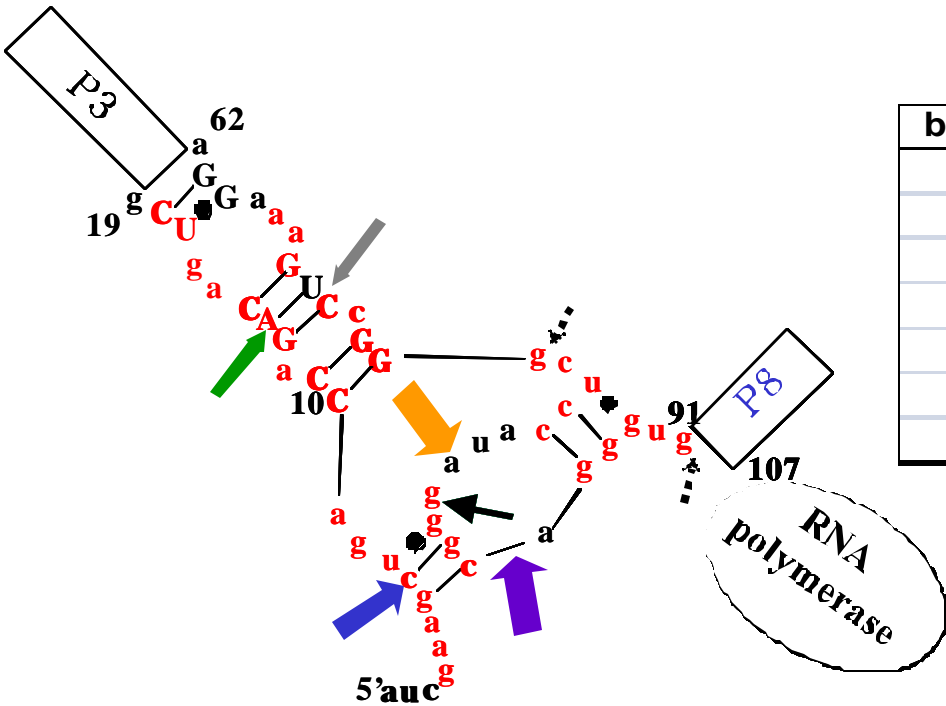


Its location: right after the 5' portion of all long-range helices!

Pausing at 119 matters to folding



An extensive paused complex structure forms (structural mapping and phylogeny)



base #1	base #2	Base Pairs	Mismatches
9	73	30CG ; 8 UG ; 1 UA	0
10	72	25CG ; 14 UG	0
12	70	37GC	2
13	69	29AU ; 10GU	0
14	68	35CG ; 4UG	0
17	64	36UG ; 3CG	0
18	63	38CG ; 1UG	0

*Core of the structure is
phylogenetically conserved . . .*

*Structure of the paused
complex matters*

Why should this non-native structure help folding?

Prevents super-stable non-native structure from forming.

It's labile, easy to undo for native structure when downstream partners are transcribed.

Provides a topological benefit for the order of strand invasions.

Recap

Long-range helix: cool for native structure, not cool for folding.....

Non-native structure in folding: can be good, can be bad; devils are in the details

Pausing matters: location, location, location

(Poster) Two other non-coding RNAs need pausing, too.

(Poster) Pause sites are conserved in related bacteria species.

Evolutionary cross-talk?

Non-coding RNA sequence/structure co-evolves with the properties of their transcribing RNA polymerase?



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Tobin Sosnick

Discussions, insights, reagents:

Robert Landick (U. Wisconsin)

Sean Eddy (Janelia Farm, HHMI)

NIH