Influence of accessibility on RNA interactions

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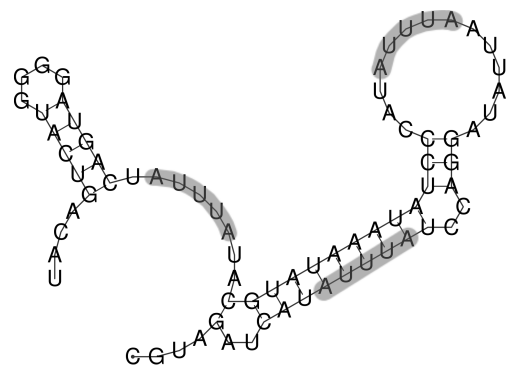
Accessibility and RNA interactions

- Our understanding is that RNA interactions require the corresponding stretch of RNA to be unpaired, i. e. accessible to interactions
- Or that the interaction requires a certain structure motif to interact, i. e. the absence of accessibility



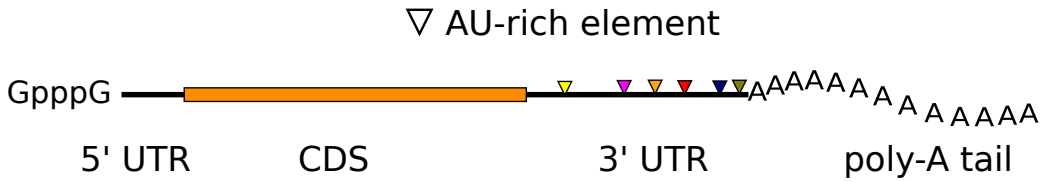
Well that sounds easy

- We measure accessibility as probability of being unpaired
- We are able to calculate this property for a stretch of RNA (e. g. RNAplfold)
- This is often used to investigate binding motifs of interaction partners
- But today I want to talk about something else

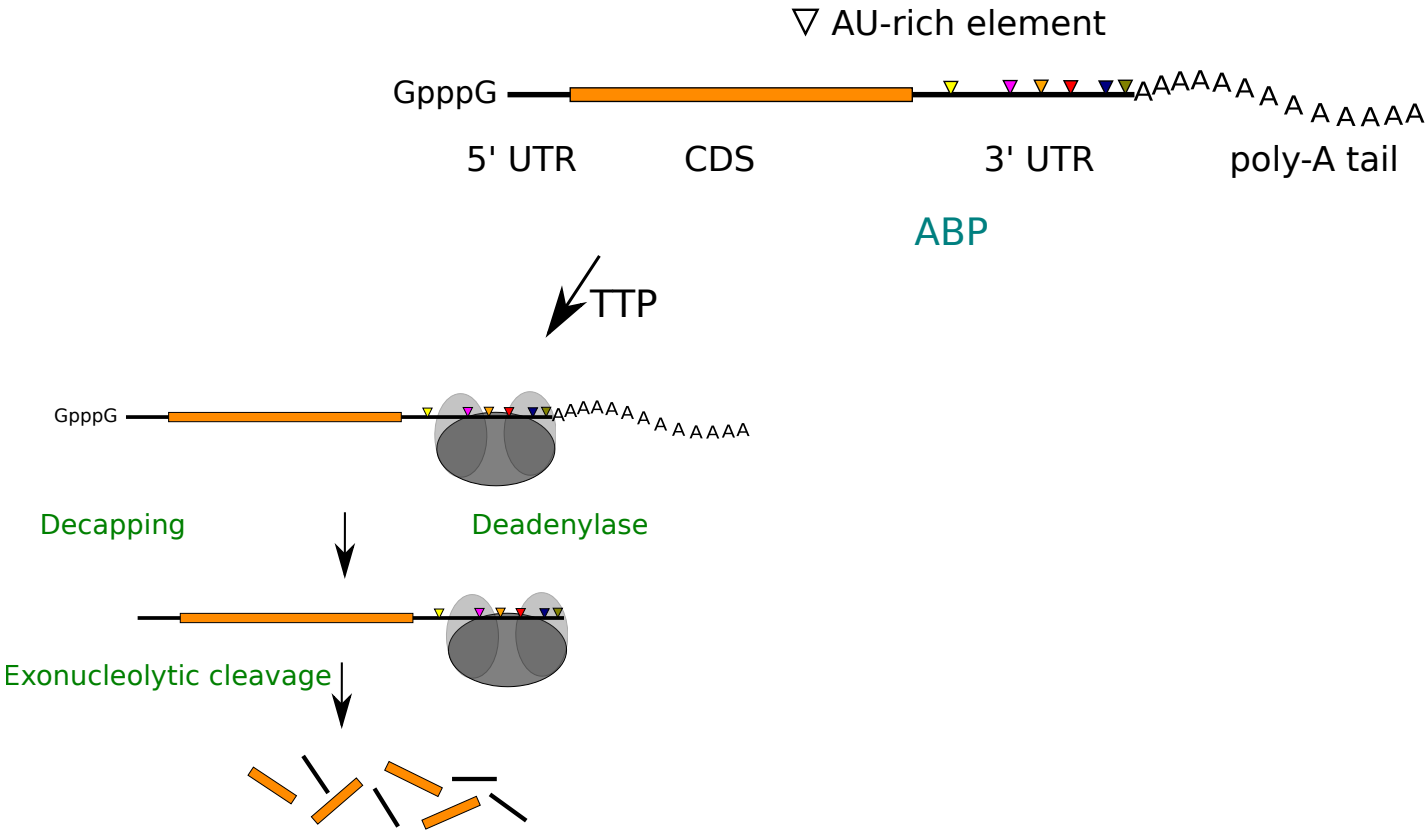
RNA - protein and RNA - RNA interactions

- Usually a molecule of RNA and the potentially interacting molecule are not alone
- The (stable) interaction does not happen just for fun but tends to have some kind of regulatory effect
- There are many many things we can learn from interaction data
- One challenge I find particularly interesting $\rightarrow$cooperation/competition

Once upon a time ...



Once upon a time ...



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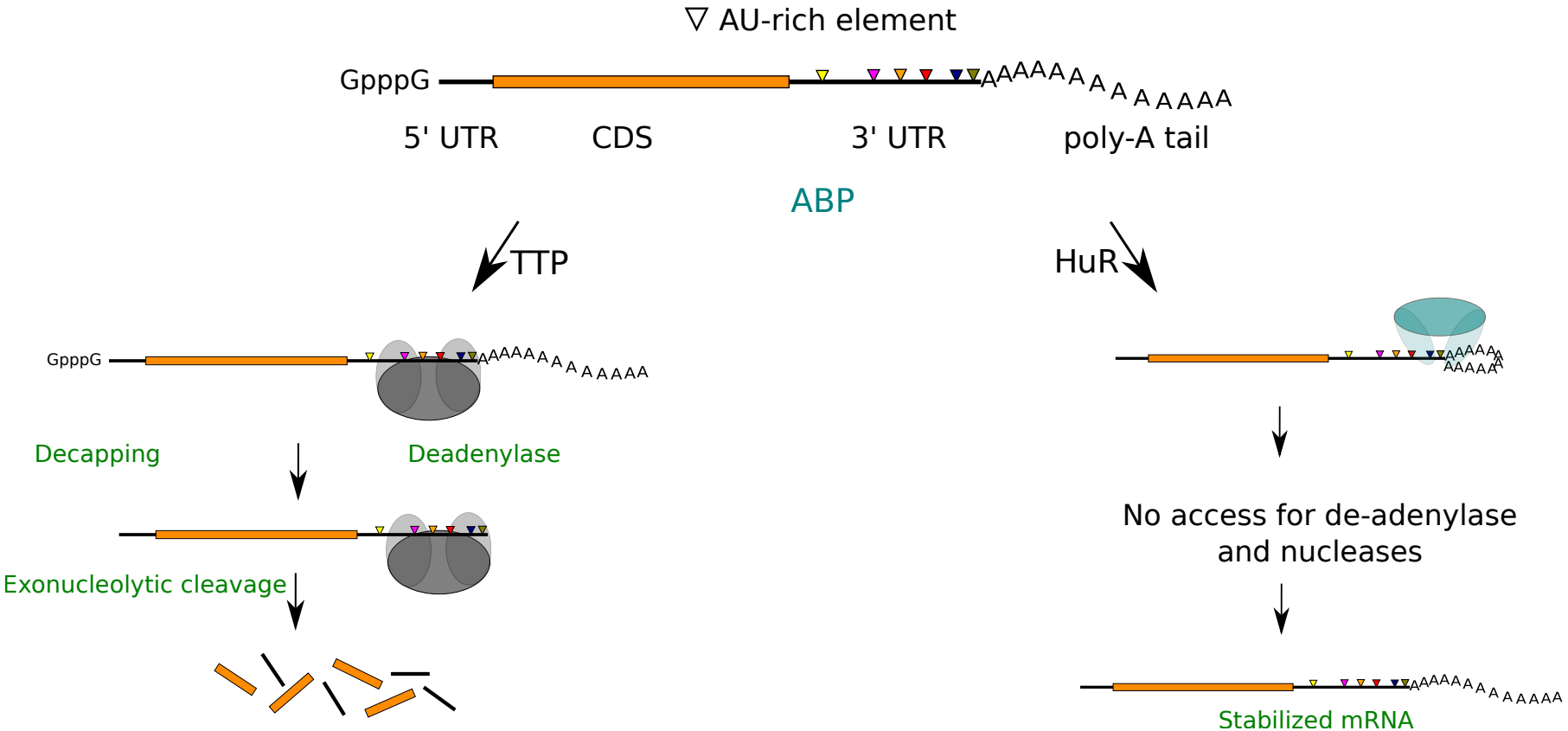

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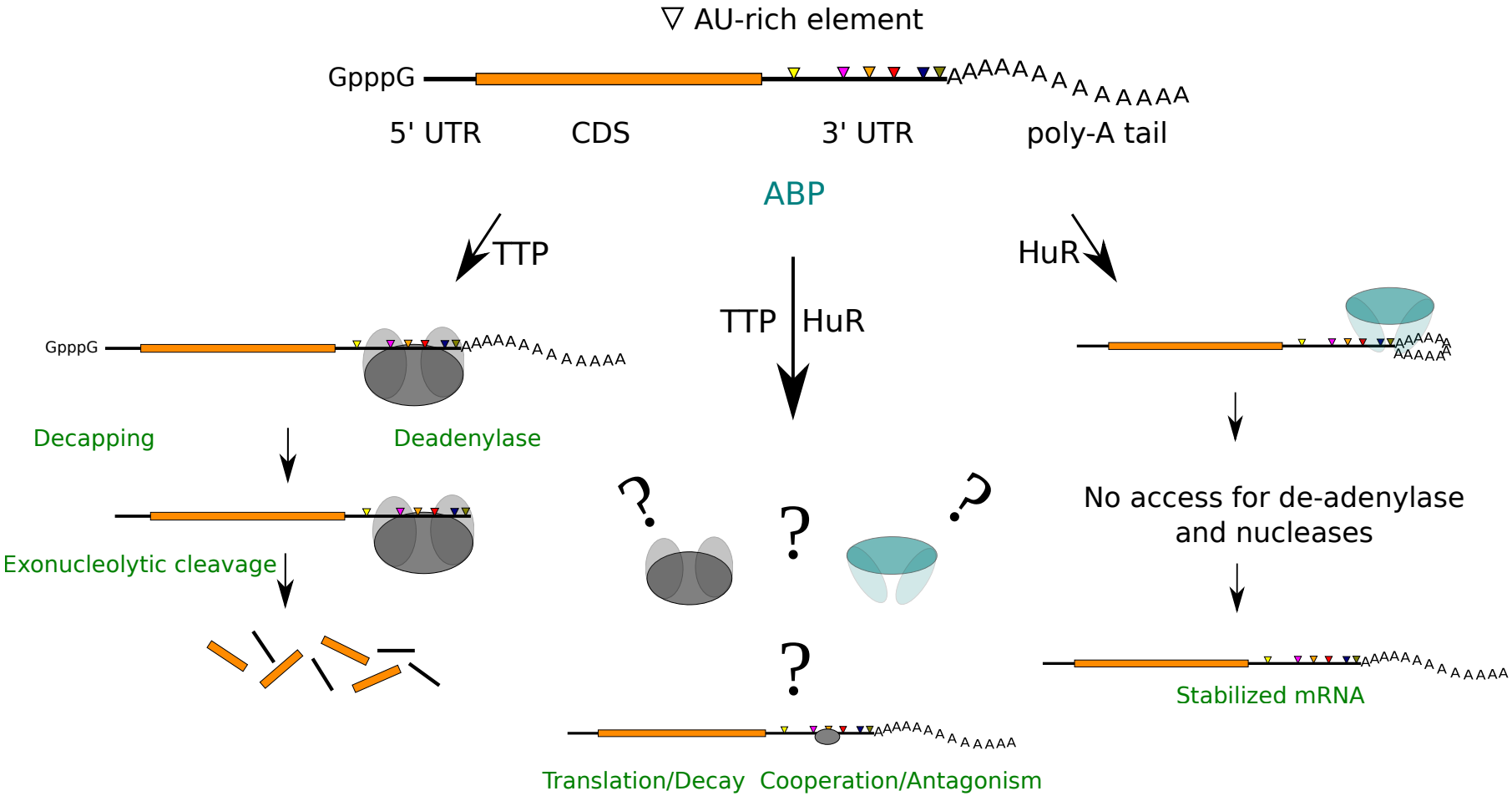


The tale continues

- Some binding sites overlap, indicating antagonism, but most don't
- They very often share targets and their effects indeed are competitive
- So what I'm interested in currently is if the binding itself can be enough to prevent the antagonist from interaction
- Or make other binding sites of the same or cooperative binders more accessible

Constraint folding, hurrayyy

- I use the very new constraint folding framework of RNAplfold to infer up/downstream regions that become more/less accessible due to interaction
- This I hope, gives me a hint about the role of RNA secondary structure as mediator of competition/cooperativity in RNA interaction

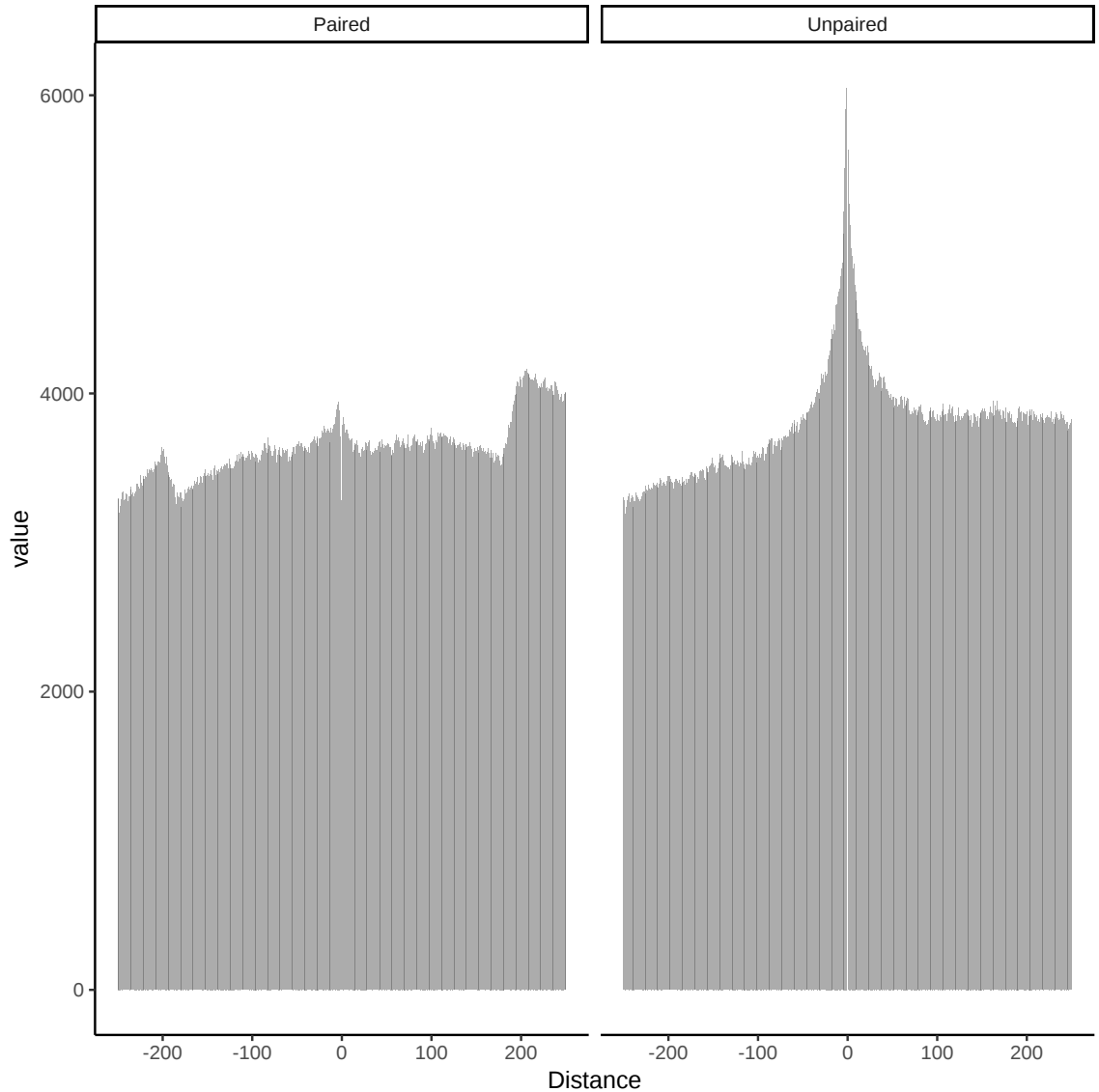
Workflow

- Derive regions of interest from CLIP data
- Predict accessibility of sequences around this region
- Repeat with CLIP-site constraint to paired/unpaired
- Compute difference in accessibility w/o constraint
- Find regions where the difference is above/below threshold
- Intersect this regions with same/other datasets

Results

Even more results

ETA soonish



Challenges

- CLIP data is noisy and binding sites vary in size →integrate motif info/miRNA seeds, toeprint
- Define a sensible cutoff →folding at temperature range, IDEAS???
- Find more known examples for cooperation/antagonism and investigate those
- Precompute accessibility profiles for mRNAs to speed up

Thanks

Ronny, Peter, Melmak, You

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