Efficient pseudoknot partition functions:

Results and (still some) open problems

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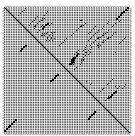
Non-crossing RNA partition functions

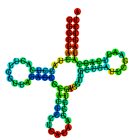
MFE prediction $\min_S E(S)$ $O(n^3)/O(n^2)$ [*Zuker*]

⇓ DISAMBIGUATION

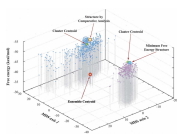
Partition Function $\sum_S \exp(-E(S)/RT)$ $O(n^3)/O(n^2)$ [*McCaskill*]



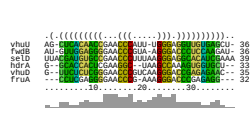
Base pair probabilities



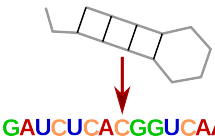
Local reliabilities



Structure sampling, Centroids, ...



RNA Alignment à la LocARNA

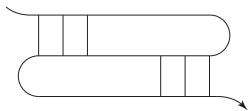


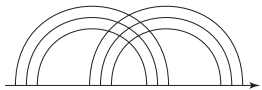
RNA Design: Pr, Ensemble defect, ...

Zuker, Stiegler 1981; Zuker, Sankoff 1984; McCaskill, Biopolymers 1990

Dirks&Pierce and the path to PK partition functions

- Simple pseudoknots





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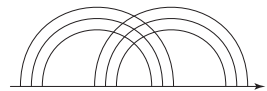

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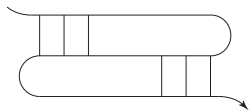

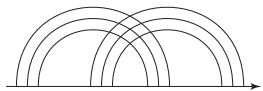

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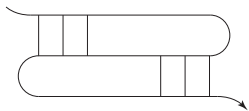

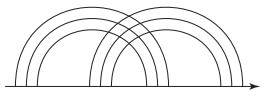

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- Implementation in NUPACK

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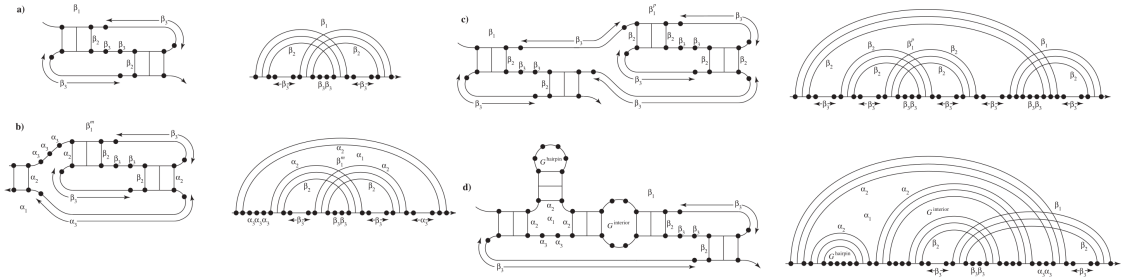
Dirks&Pierce / Hotknots 2.0 energy model



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- Turner NN + additional parameters: external/internal pseudoknot base pairs, bases in pseudoloops...
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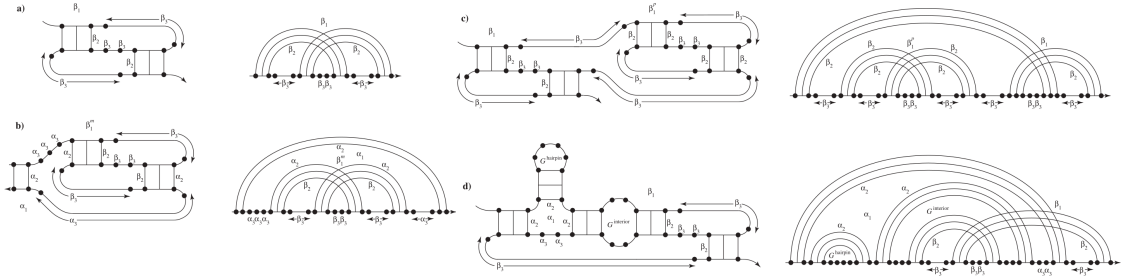

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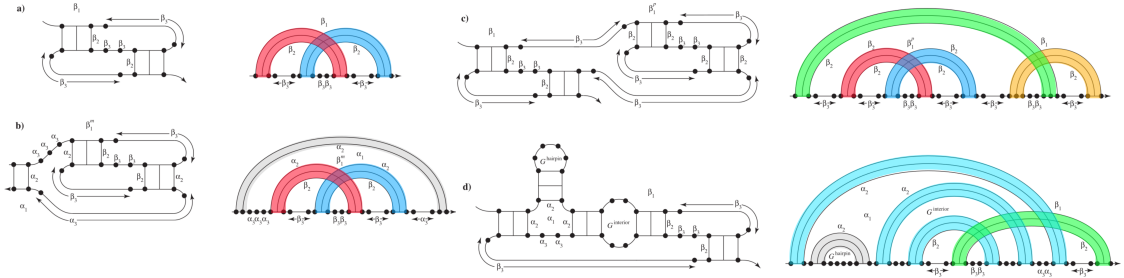

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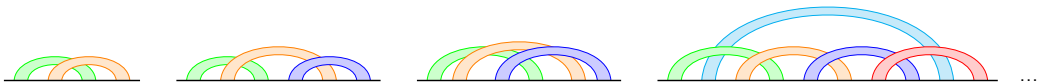
Beyond simple pseudoknots (overview)



- Partition function for CCJ pseudoknots (or Rivas/Eddy pseudoknots)
  Pseudoknot classes motivated by computational complexity; "gap grammars"
- Partition functions for Fatgraphs/Shadows
  Controlled pseudoknot classes defined by sets of band configurations
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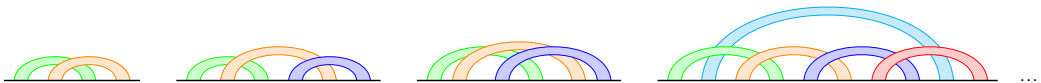

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CCJ partition function

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- DP algo idea: 

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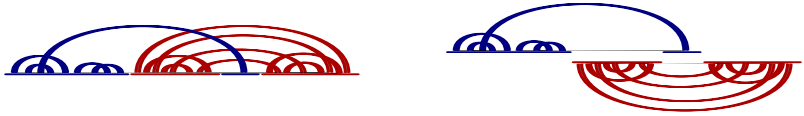
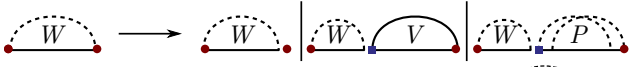
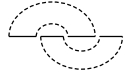


- DP algo idea: 

  - Compose CCJ PKs from two "1 gap" TGB fragments 

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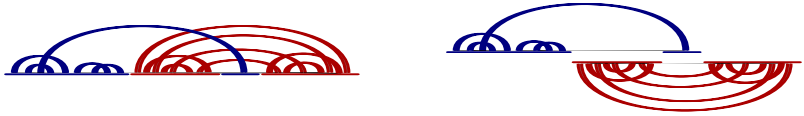
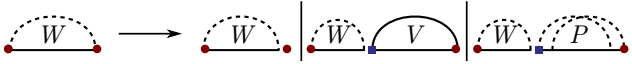


- DP algo idea: 

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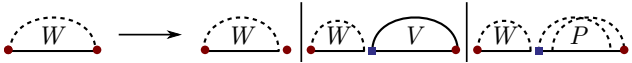
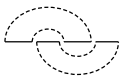
- DP algo idea: 

  - Compose CCJ PKs from two "1 gap" TGB fragments 
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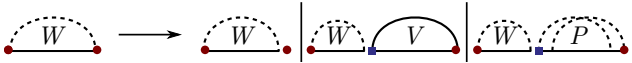
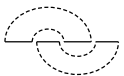
- DP algo idea: 

  - Compose CCJ PKs from two "1 gap" TGB fragments 
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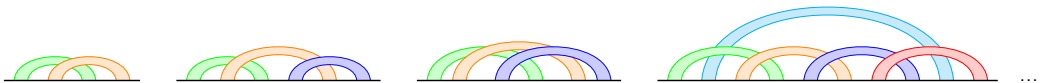

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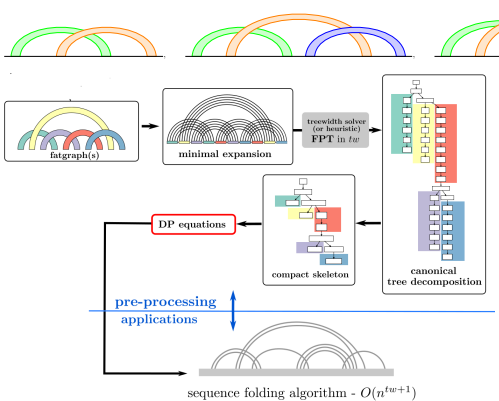
Automatically generated algos based on fatgraphs

Recursive PK of controlled "band" configurations / topology



- Gfold: mfe + partition function for 1-structures
  manual rewriting of grammar rules per fatgraph
  e.g. $P_{KHP} \rightarrow A_1 IB_1 IA_2 IC_1 IB_2 IC_2$ "$O(n^{12})$"
- AutoDP automates grammar rewriting
  by tree decomposition
- in progress: full energy function, disambiguation, algebra exchange

Reidys et al., Topology and prediction of RNA pseudoknots. Bionformatics, 2011.

Marchand et al., Automated design of DP schemes for RNA folding with pseudoknots. ALMOB, 2023.

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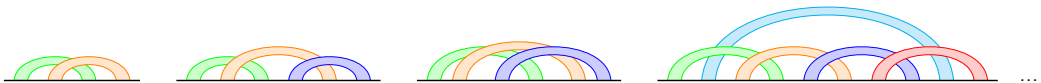

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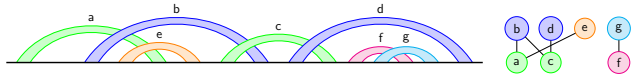

- **HFold**: Hotknots 2.0 MFE of bi-secondary "densitity-2" structures

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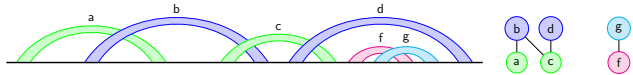

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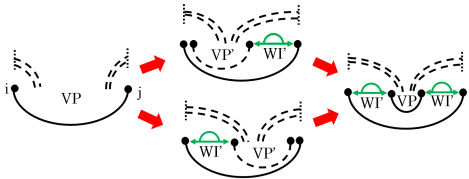

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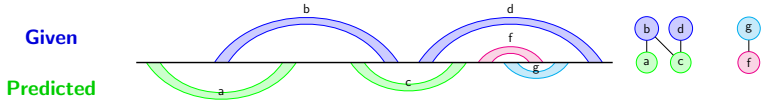

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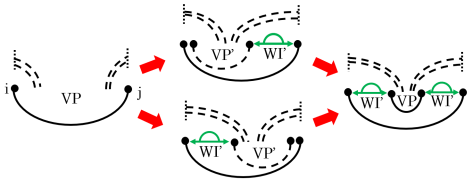

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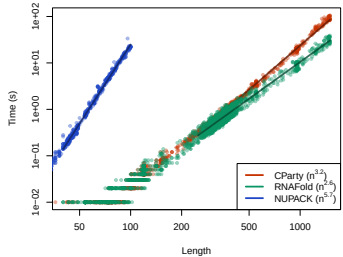

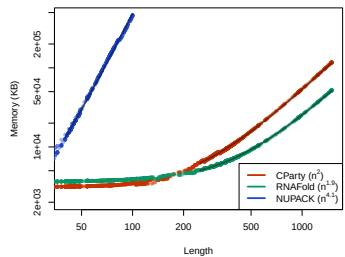

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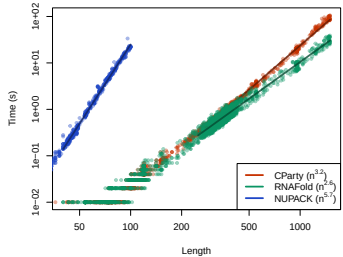
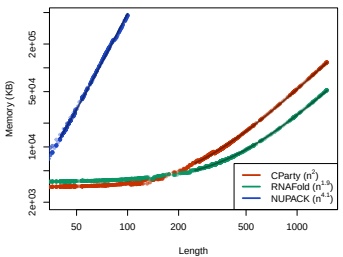
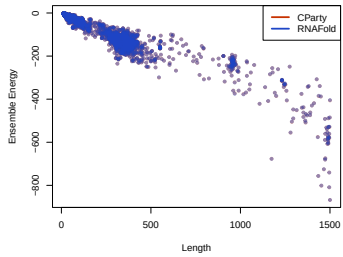
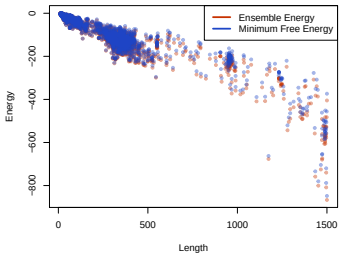




- Empirical Validation





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Conclusions

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  bioRχiv doi:10.1101/2023.05.16.541023  github:HosnaJabbari/CParty

- CCJ partition function full energy model: *in progress*
  - challenge: disambiguation (!) → restrictions of parts of PK

- Automatically generated PF algos based on fatgraphs: *in progress*
  - less complex disambiguation compared to CCJ
  - ongoing: implementation with ViennaRNA grammar extensions + full energy model

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- CCJ partition function full energy model: *in progress*
  - challenge: disambiguation (!) → restrictions of parts of PK

- Automatically generated PF algos based on fatgraphs: *in progress*
  - less complex disambiguation compared to CCJ
  - ongoing: implementation with ViennaRNA grammar extensions + full energy model


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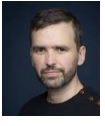
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