mRNA/siRNA Hybridzation energy and mRNA secondary structure influences on siRNA efficiency

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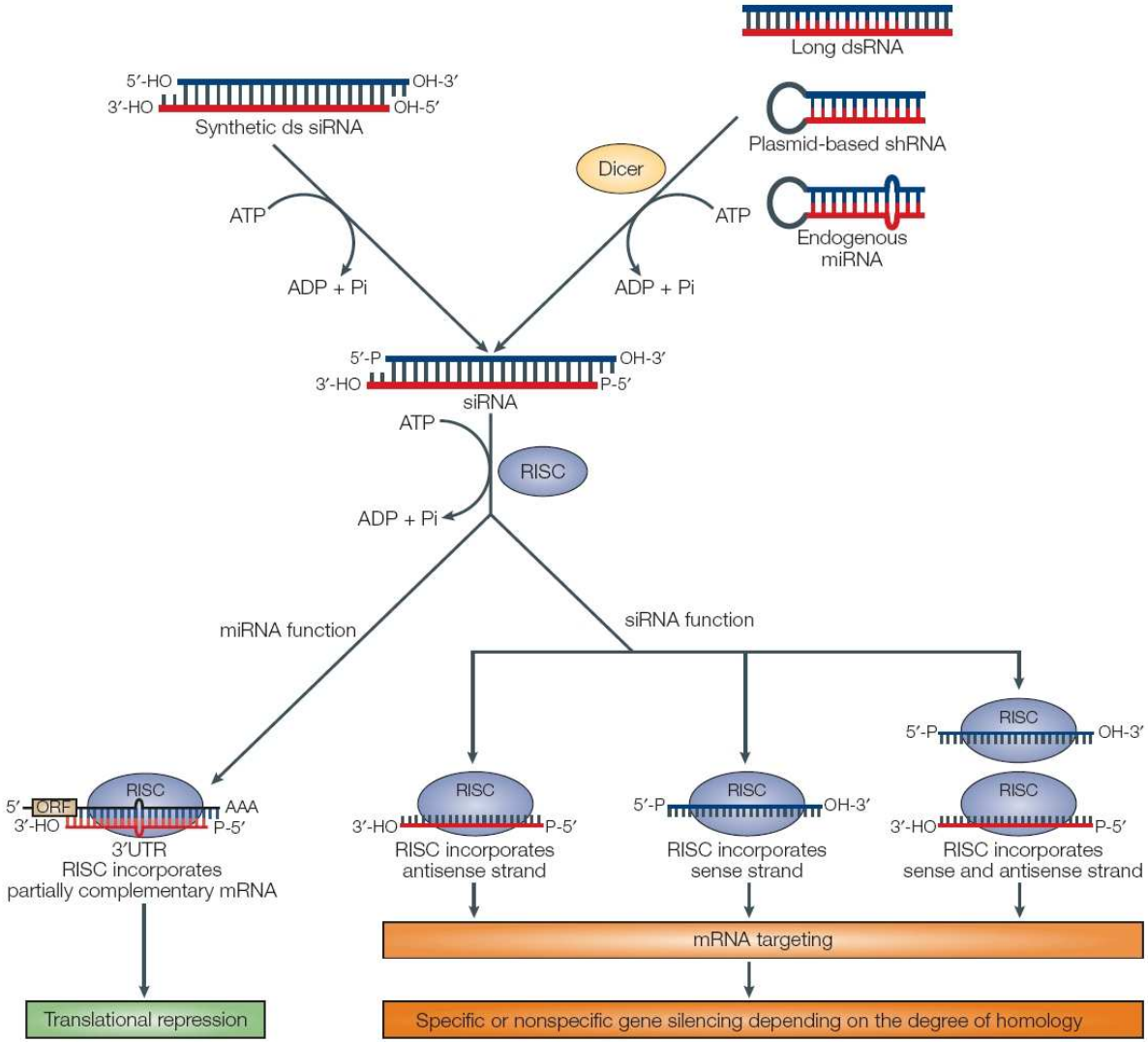
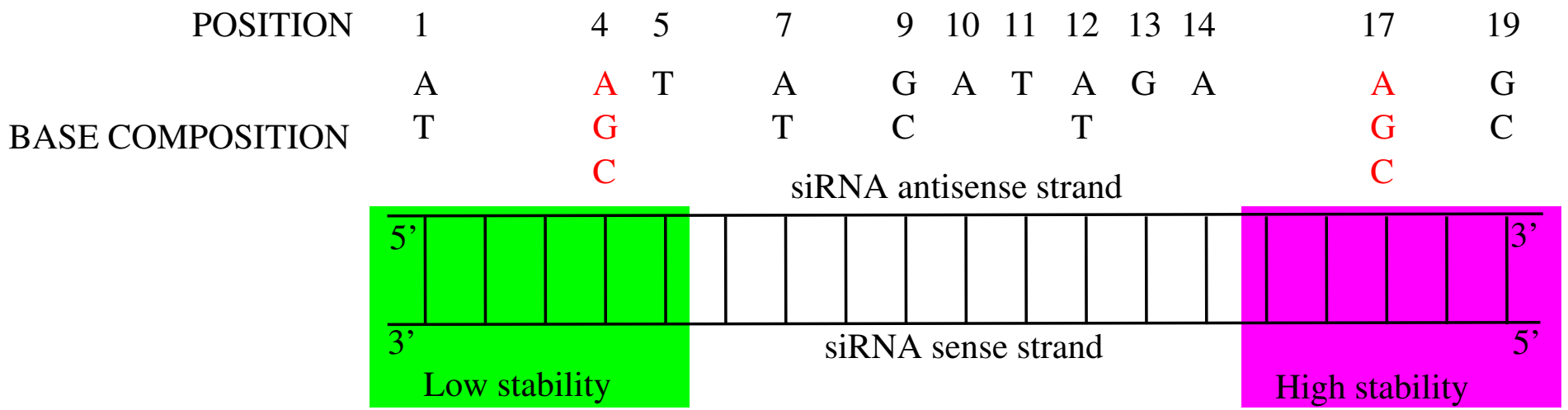
Content

- siRNA pathway
- Current rules used to improve siRNA efficiency
- Problem with current siRNA design rules
- mRNA/siRNA Hybridization Energy siRNA efficiency
- mRNA secondary structure and siRNA efficiency (Ulli)
- Conclusion

siRNA pathway



siRNA design rules



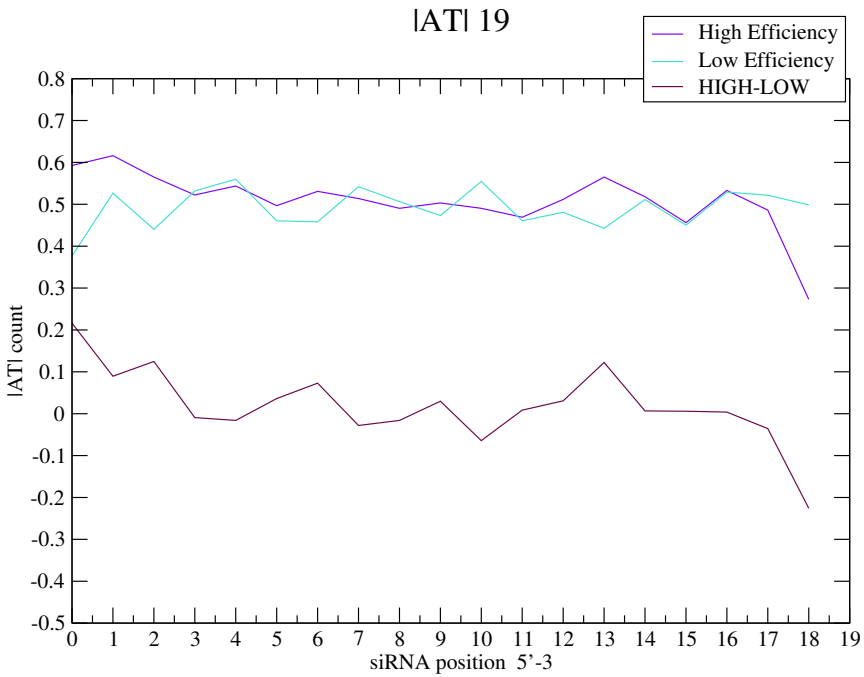
siRNA design rules

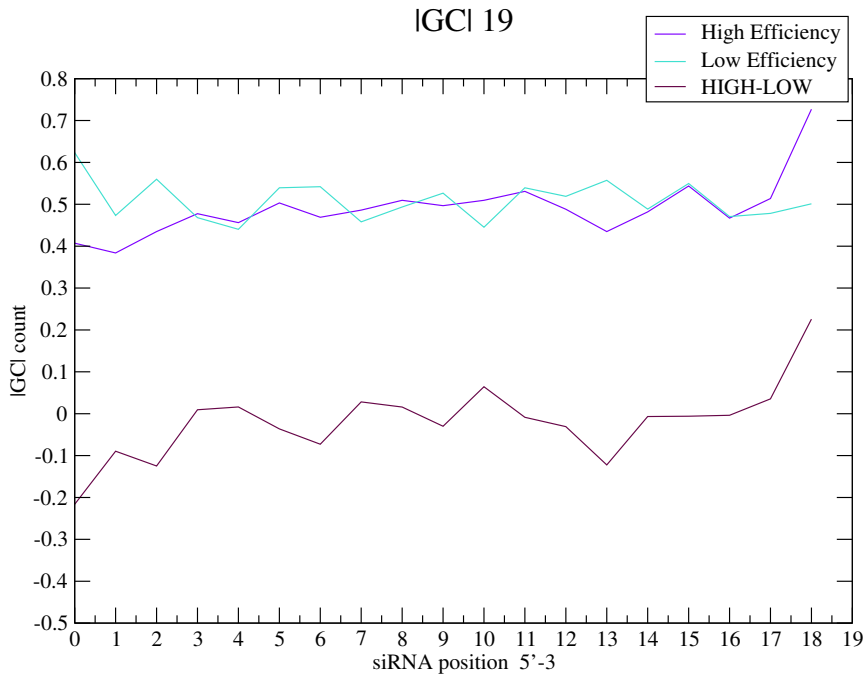
- Based on small datasets 19-298 siRNA/mRNA pairs
- Do not take structure into account
- Only 20% siRNA are active by more than 90%
- Check these rules on a bigger dataset.

Dataset: siRecord

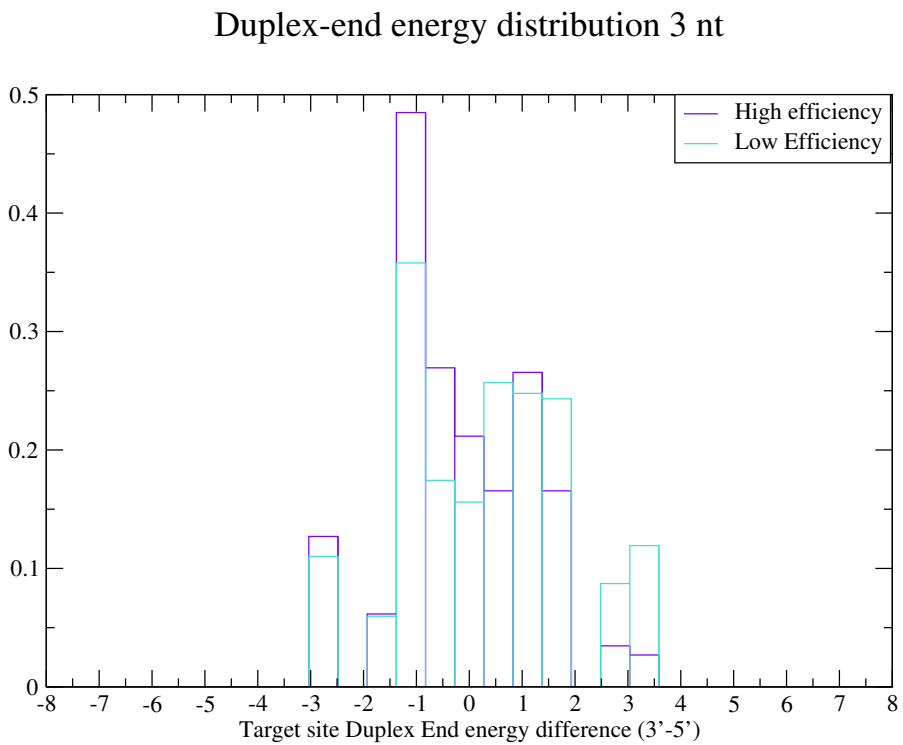
- interactions between siRNA and its target mRNA
- 975 interactions with high silencing efficiency
- 551 interactions with low silencing efficiency
- subset: HEK293VECTOR
  celltyp: HEK293; transfection via vector
  - 204 interactions with high silencing efficiency
  - 76 interactions with low silencing efficiency

sequence analysis

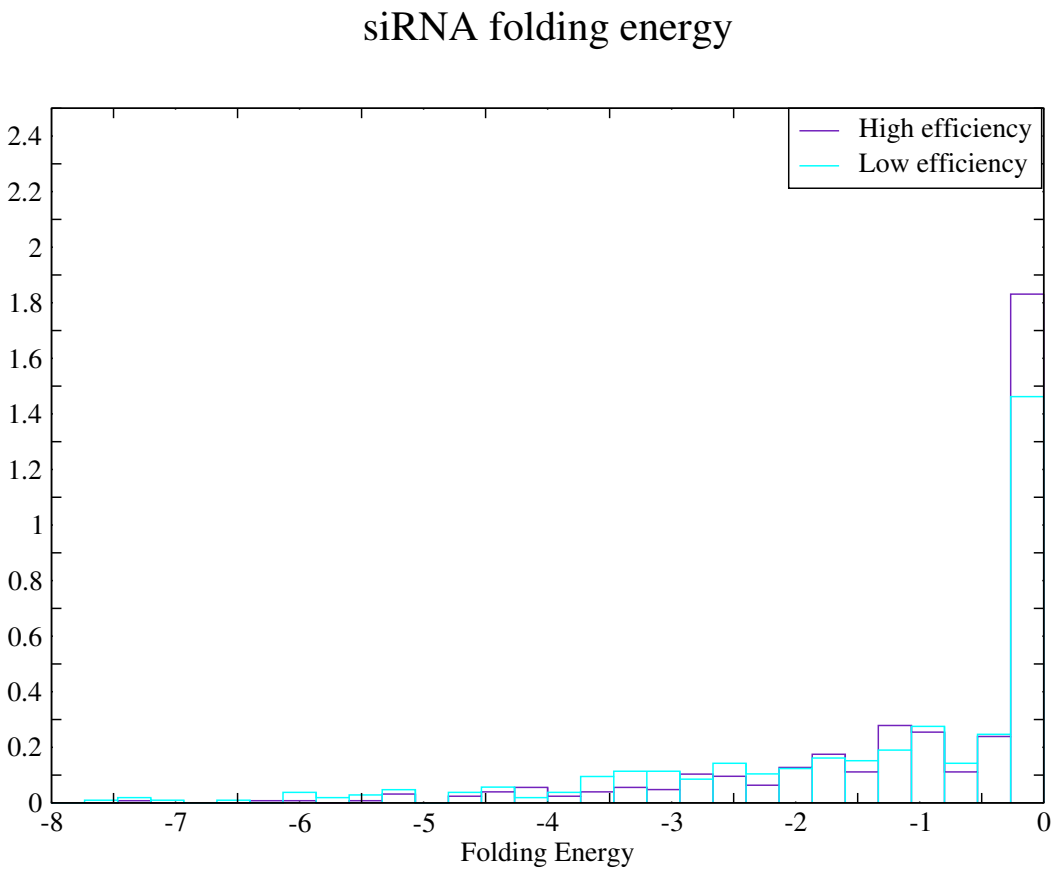




duplex end energy difference



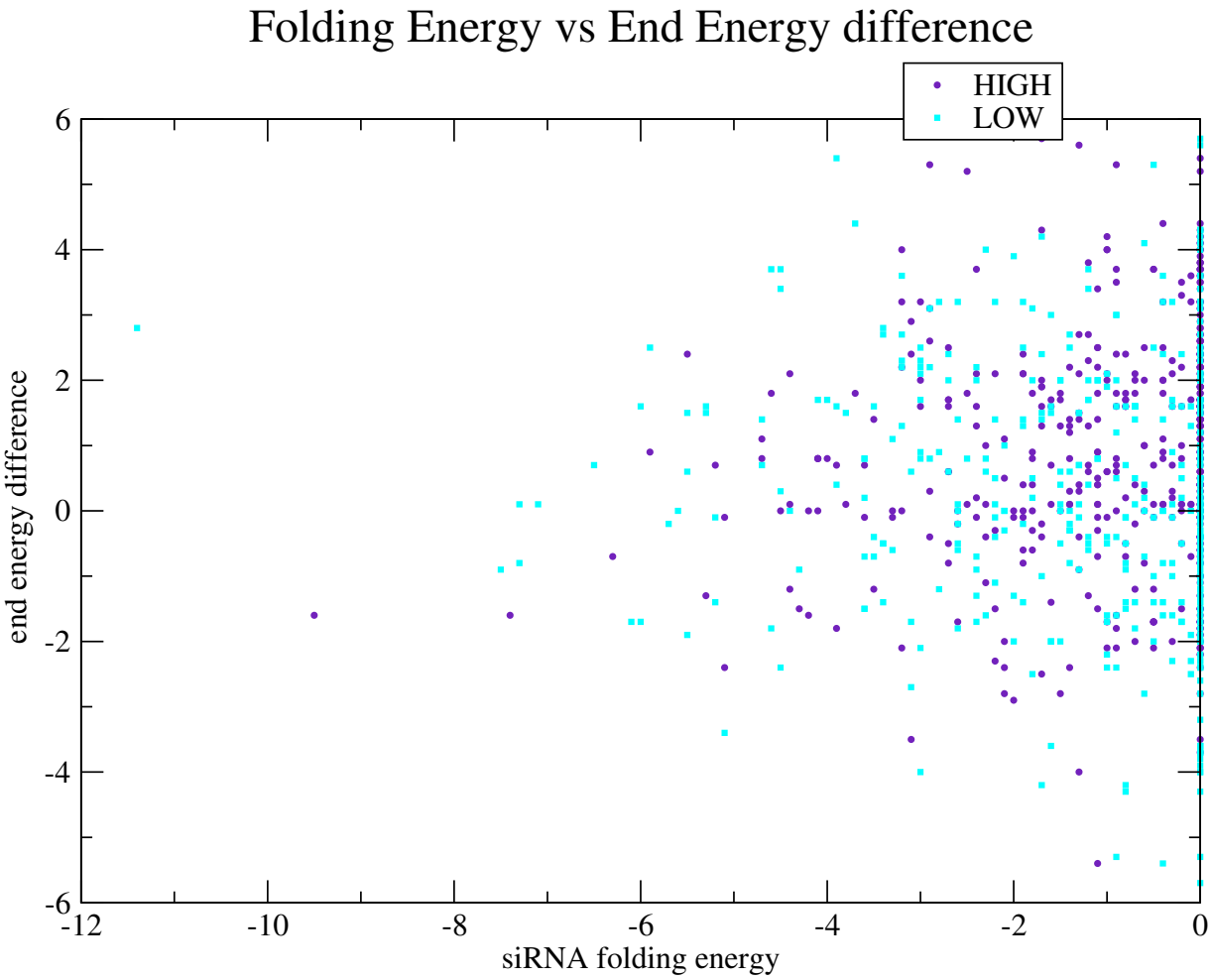
siRNA folding energy



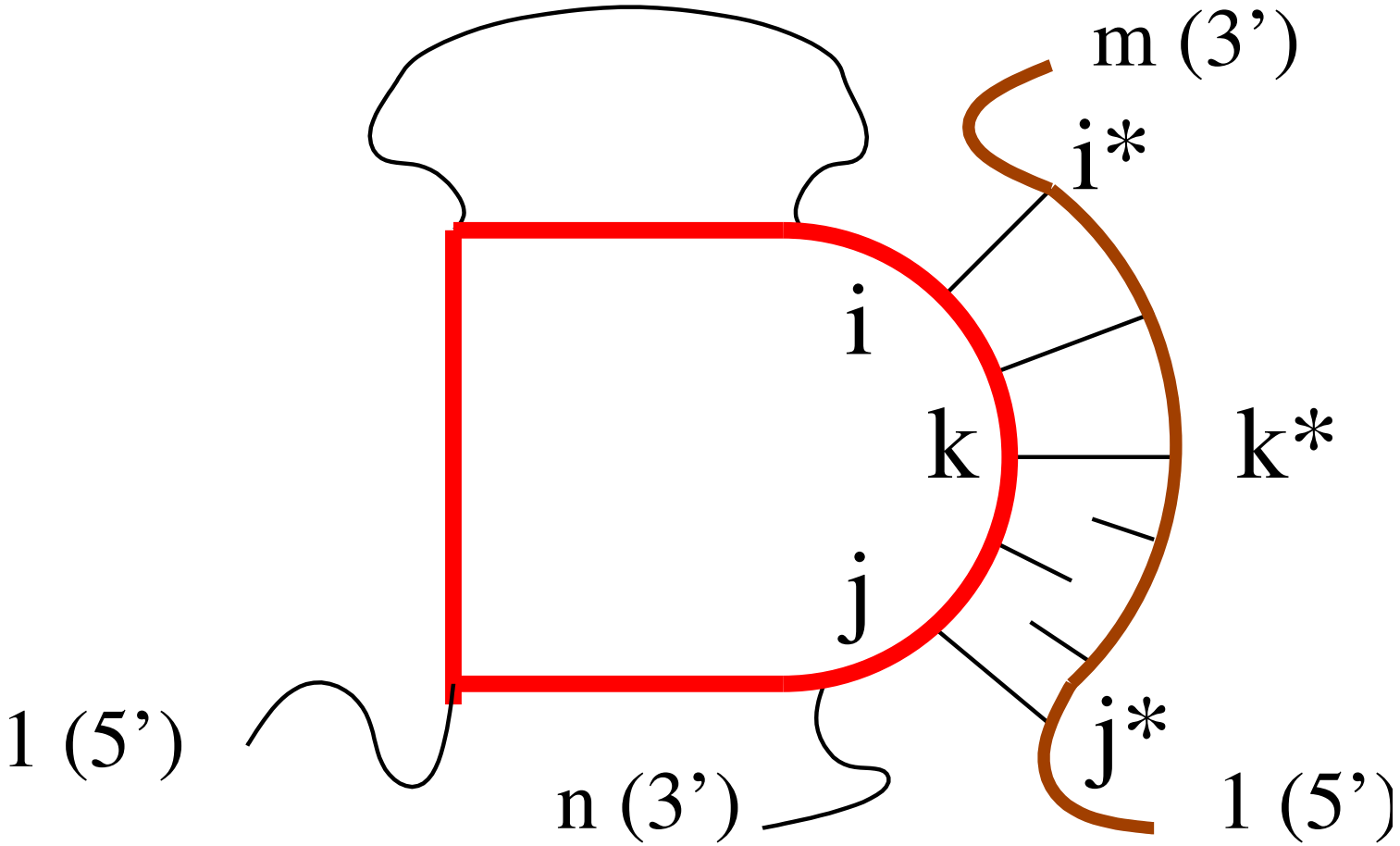
validated siRNA design rules

- siRNA efficiency correlates with duplex end energy asymmetry
- This asymmetry can be seen in the A/T C/G distribution along the siRNA
- siRNA folding energy should be small
- Other rules are not validated

validated siRNA design rules

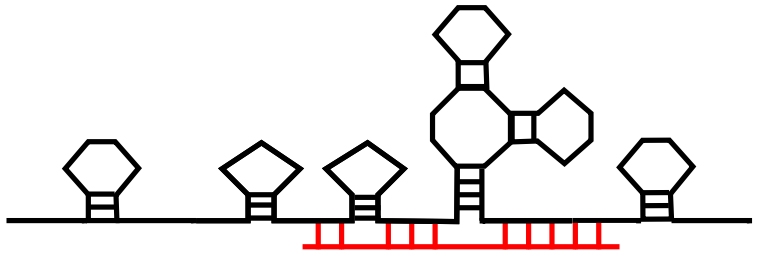


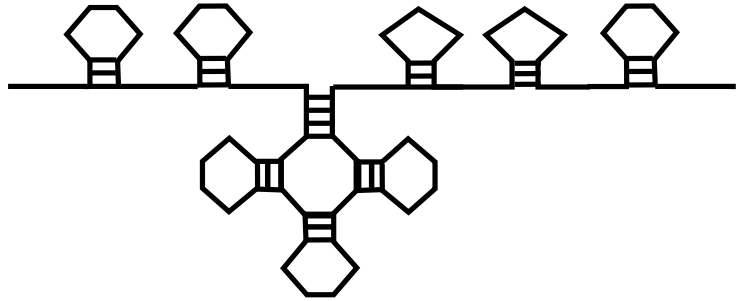
RNAup



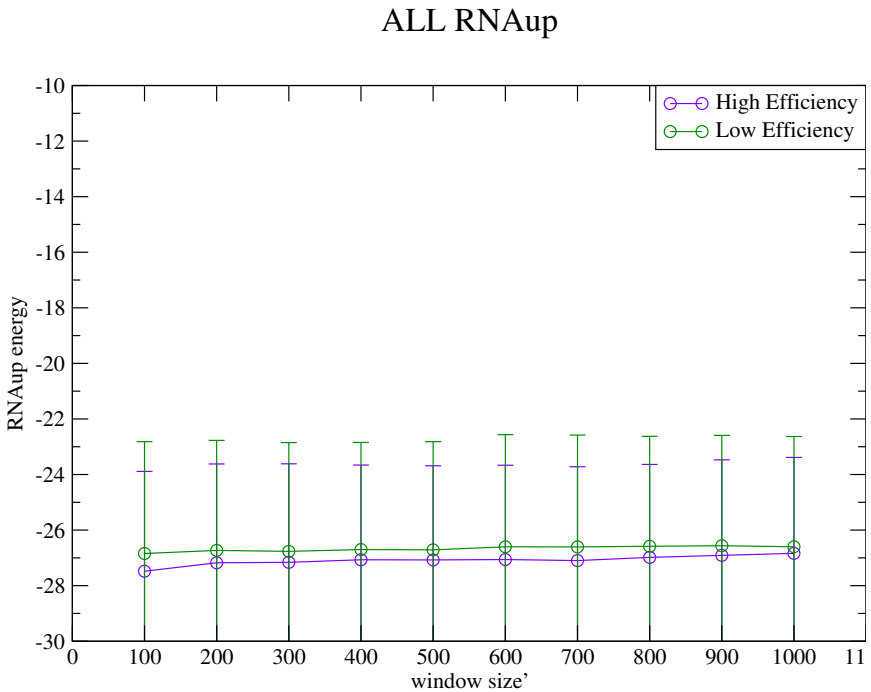
RNAcofold

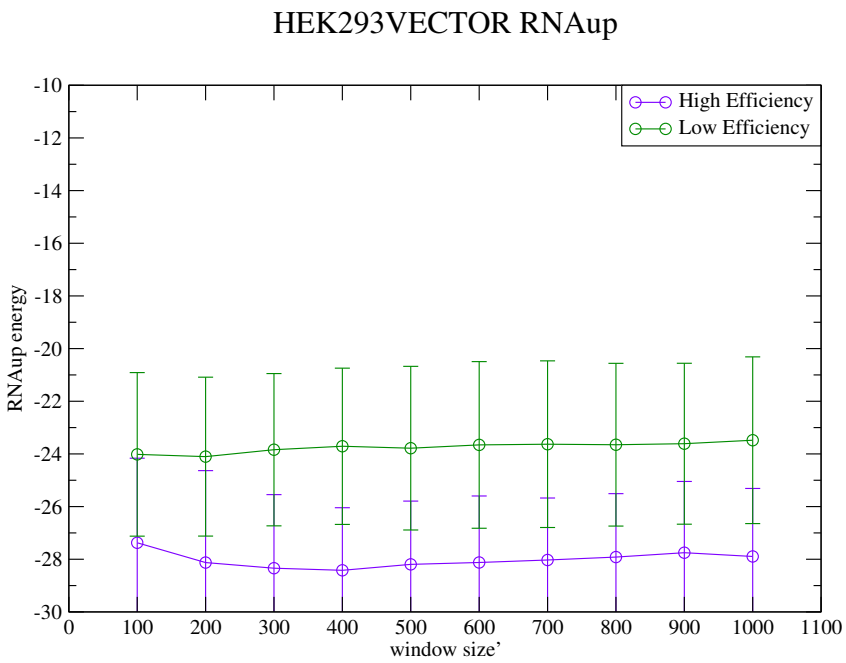
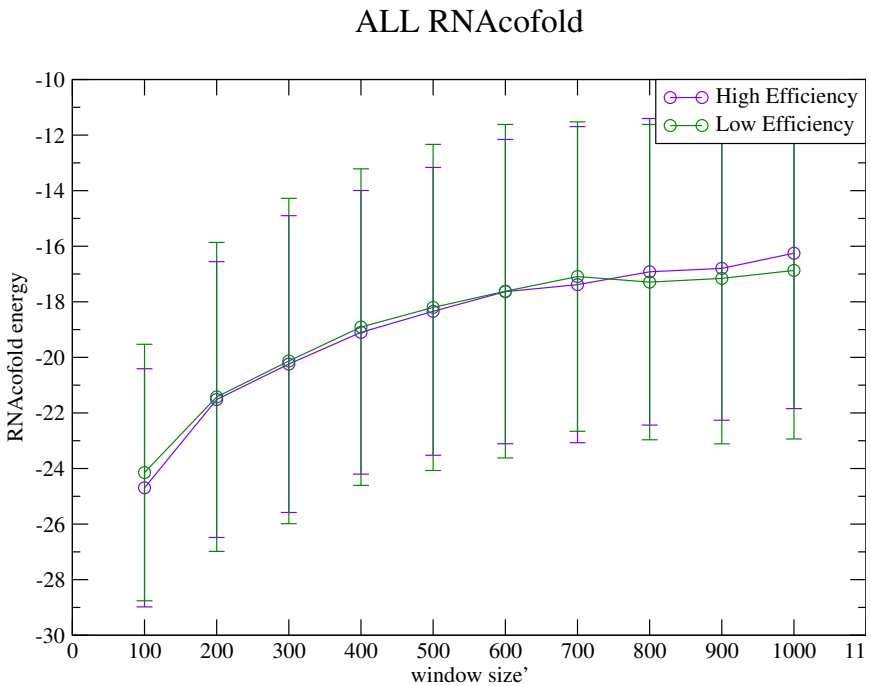
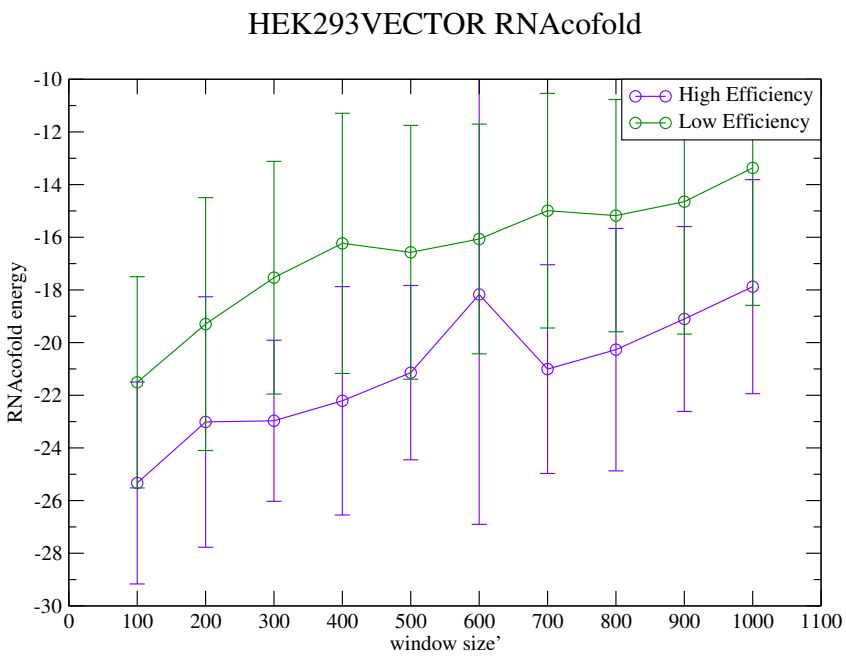
$$E_{cofold} - E_{fold} - E_{hybridization}$$





Hybridization Energy





Hybridization Energy