RNA kinetics on varying energy landscapes

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TBI Winterseminar 2009, Bled, February 15-22

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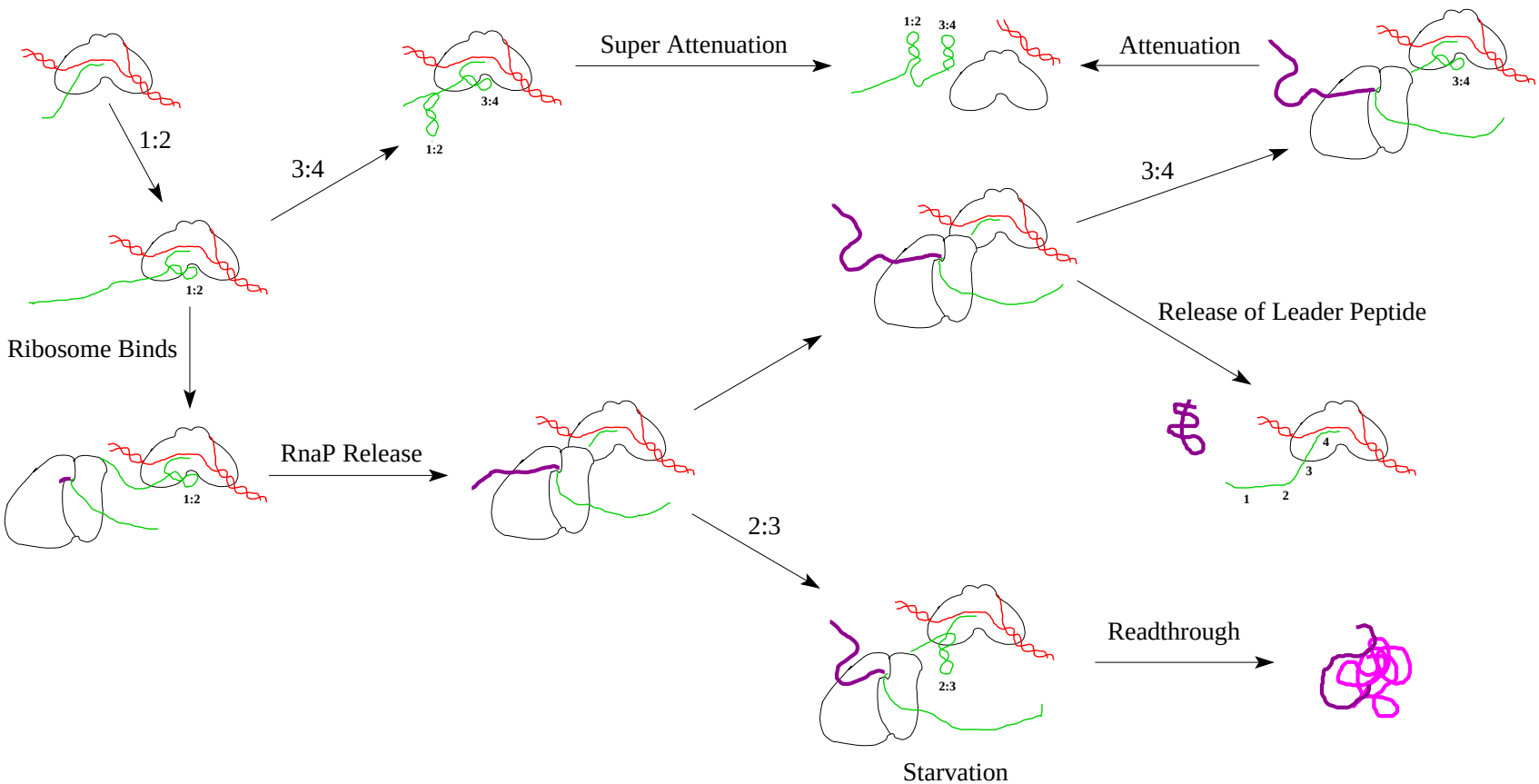
Motivation

Dynamic processes (on changing landscapes) show up all over the place.

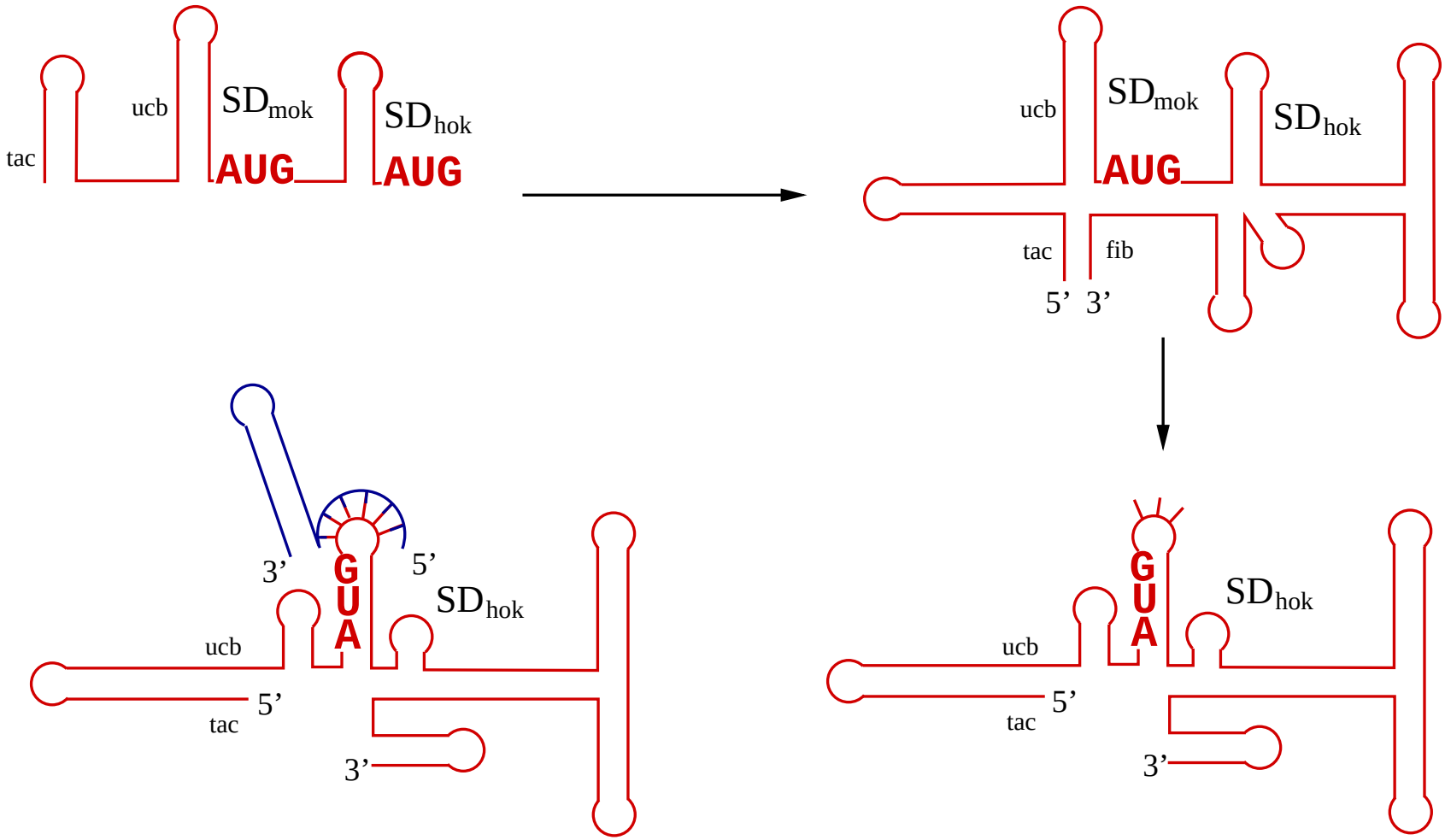
1. Natural phenomena
   - Folding during transcription (Terminator/Antiterminator).
   - Self-induced RNA switches (Hok/Soc, ...).
   - Inducable RNA switches (Riboswitches, RNA-thermometer, ...)
2. RNA/DNA based computation and nanotechnology
   - Molecular Motors.
   - Logical Gates.
   - Nano-object construction by algorithmic self-assambly.
3. Synthetic biology
   - post-transcriptional control devices.

Transcriptional Attenuation



adapted from Yanofsky, C (2000) *J Bacteriol* **182**(1):1-8

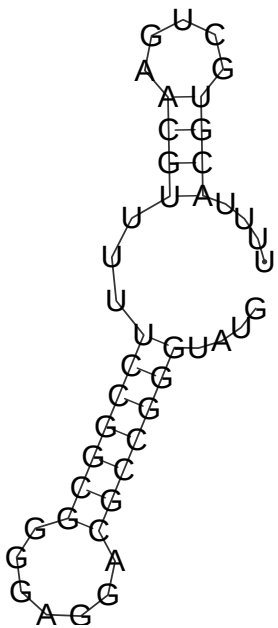
Hok/Sok – a cool natural self-induced swith

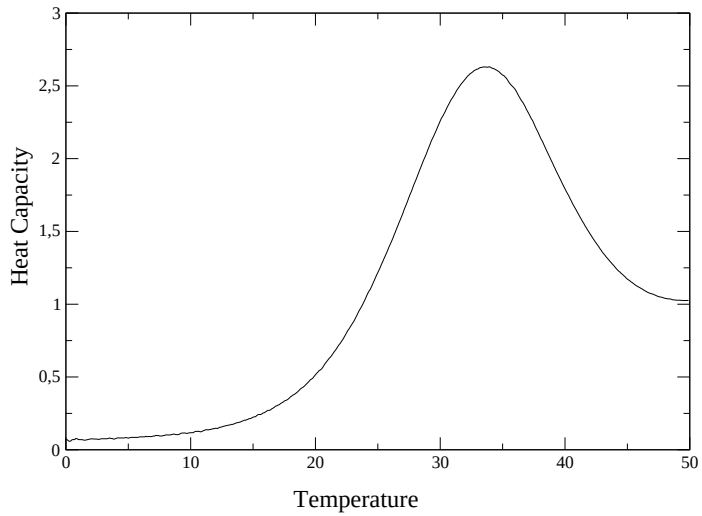


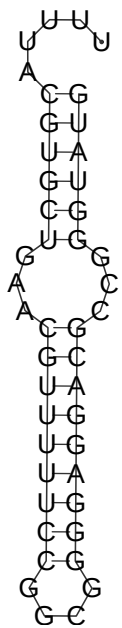
adapted from Gerdes, K & Wagner, EGH (2007) *Curr Opin Microbiol* **10**:117-124

RNA Thermometer

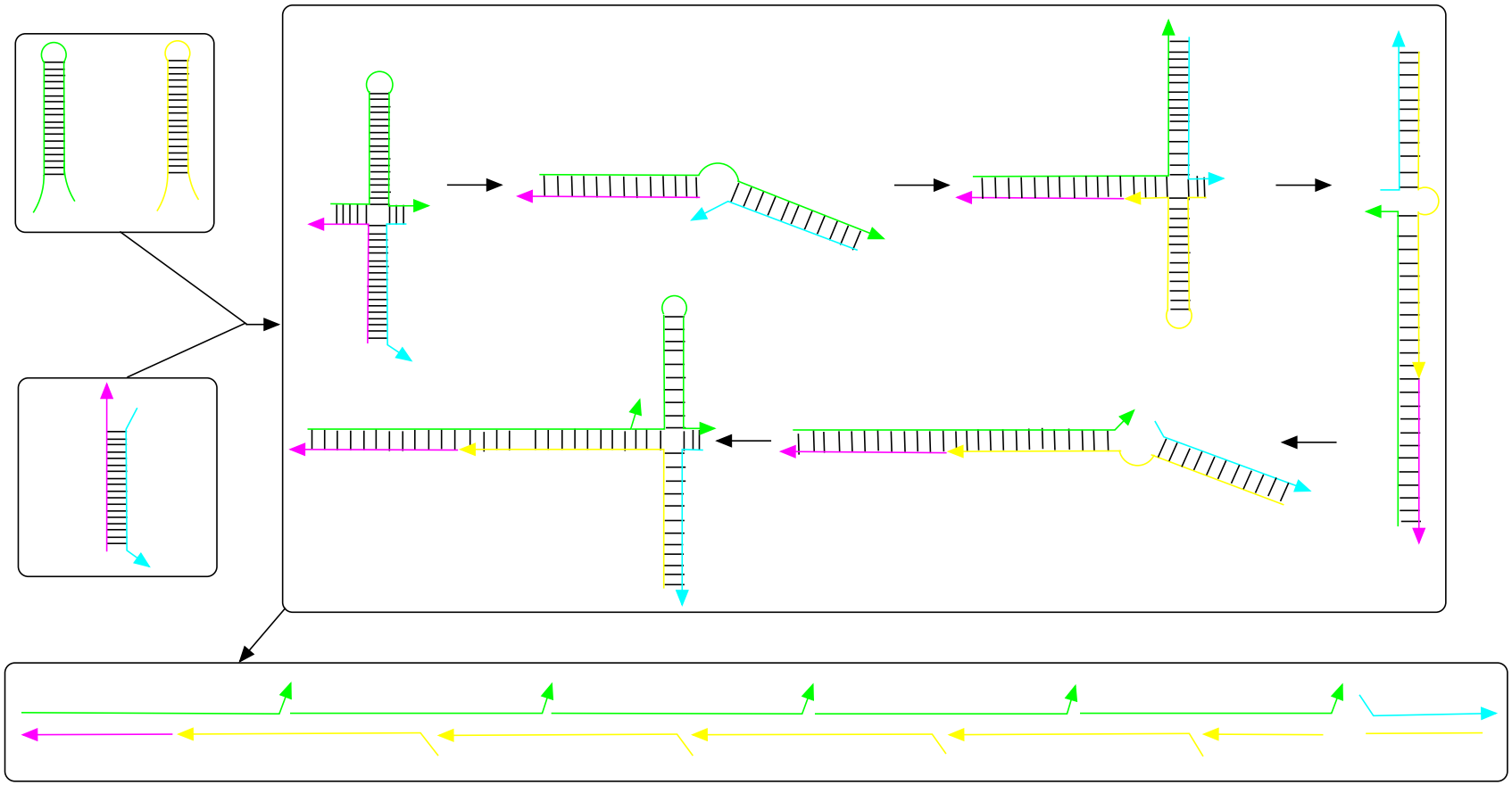
- Change structure in response to temperature changes.
- Gene regulation by masking the ribosome-binding site.
- Found in 5'-UTRs of bacterial heat shock and virulence genes.

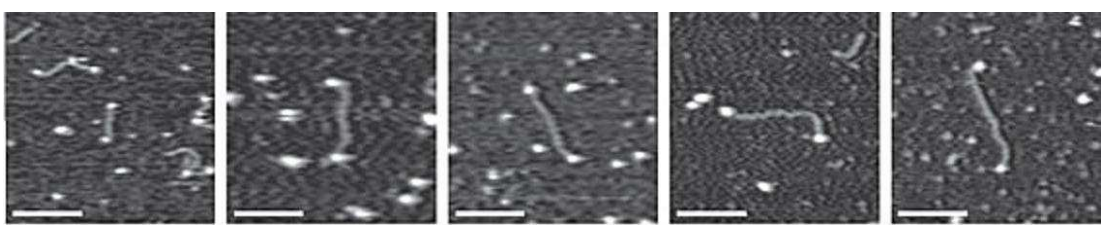


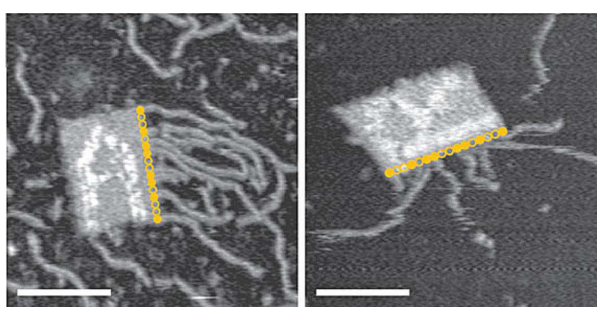




Autonomous RNA polymerization motor







Venkataraman S et al (2007) *Nature Nanotech* **2**:490-494

Basic Question

Howto handle different perturbations of the energy landscape within a **common framework**?

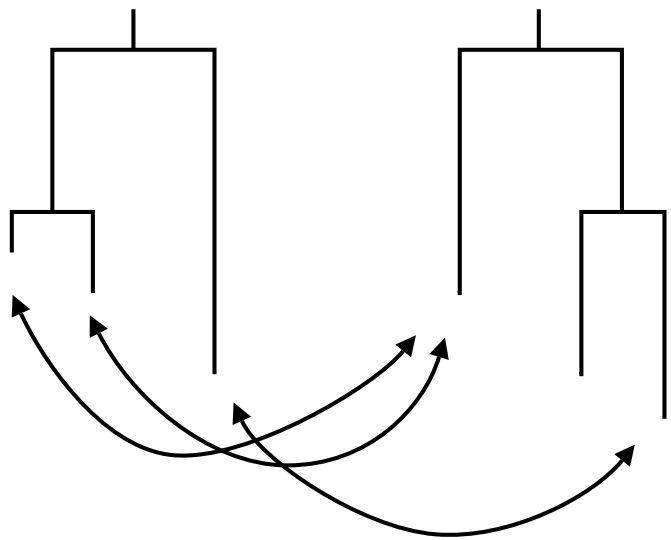
Idea:

1. Compute a sequence of barrier trees.
2. Compute mapping between local minima of conscutive barrier trees ($x \longrightarrow x' \longrightarrow$ gradient descent $\longrightarrow x^*$).
3. Simulate dynamics for a certain time on a barrier tree.
4. Map final population densities to successor barrier tree.

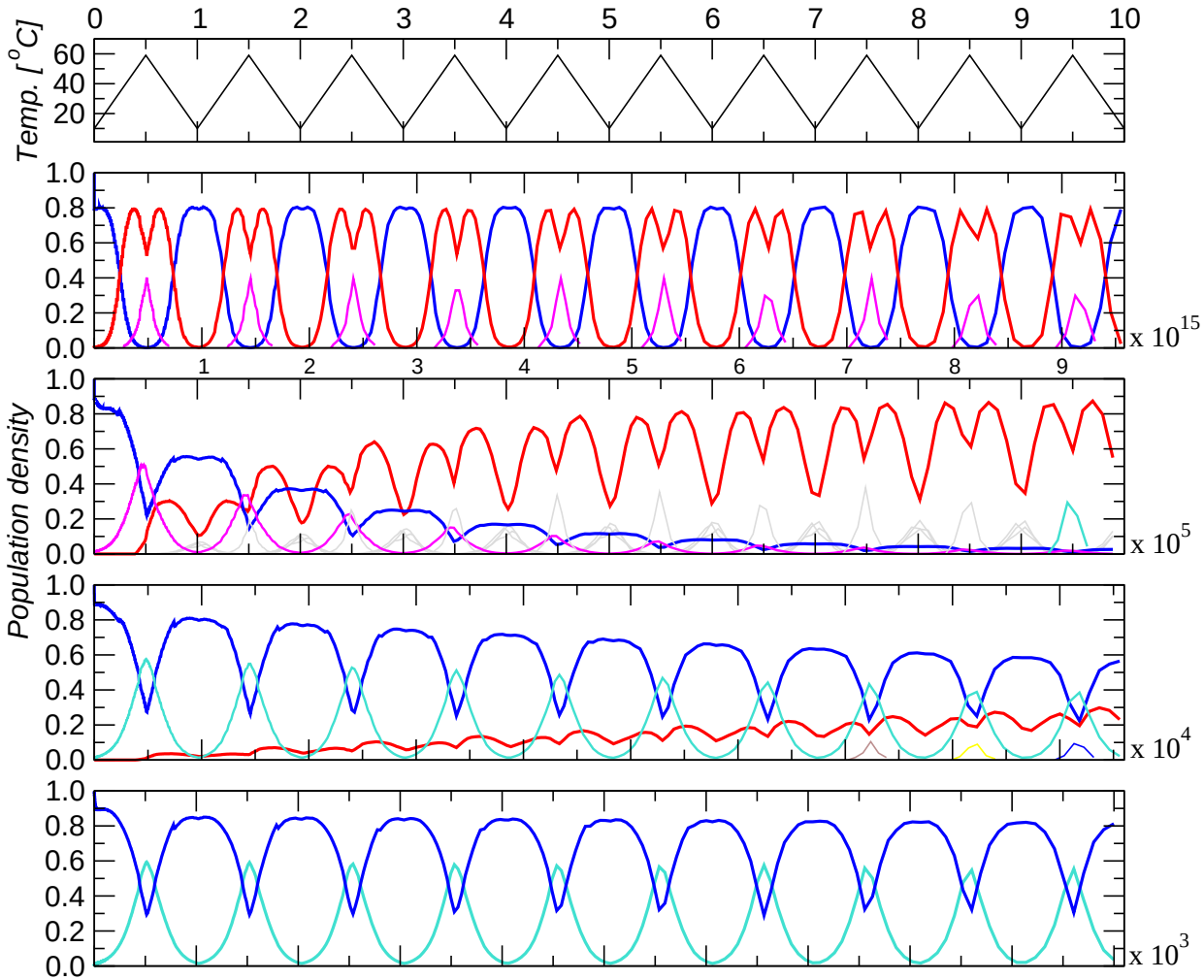
Cotranscriptional Folding

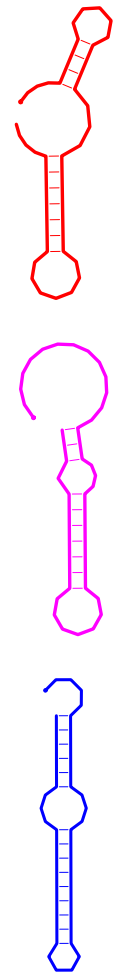
Each structure x at length n corresponds to an extended structure $x\bullet$ at length $n+1$.
For a minimum m, the correponding minimum m' can be found by a gradient walk starting with $m\bullet$.

- Two minima may be mapped to the same minimum in the $n+1$ landscape.
- In addition new minima may appear.

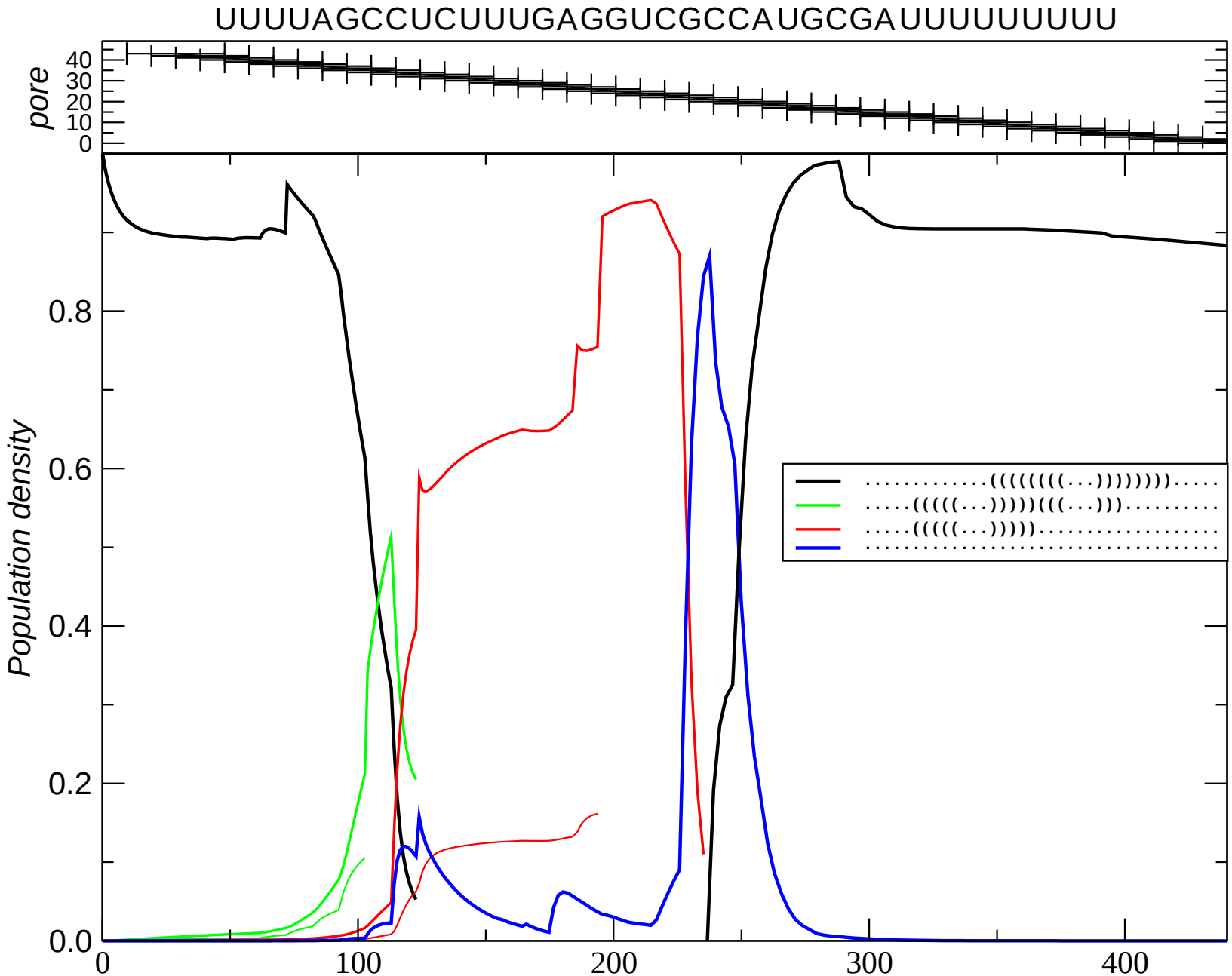


RNA thermometer: Hysteresis Effect

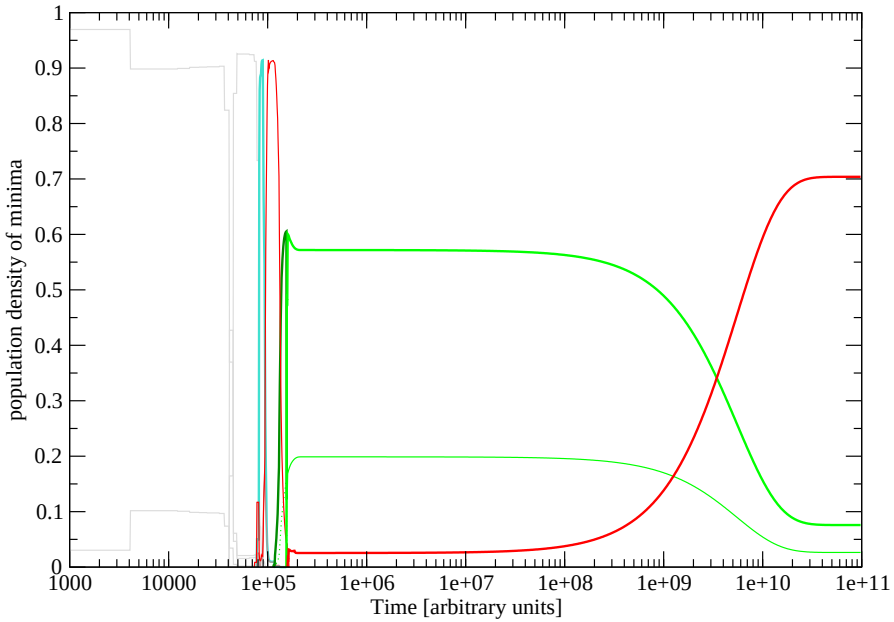


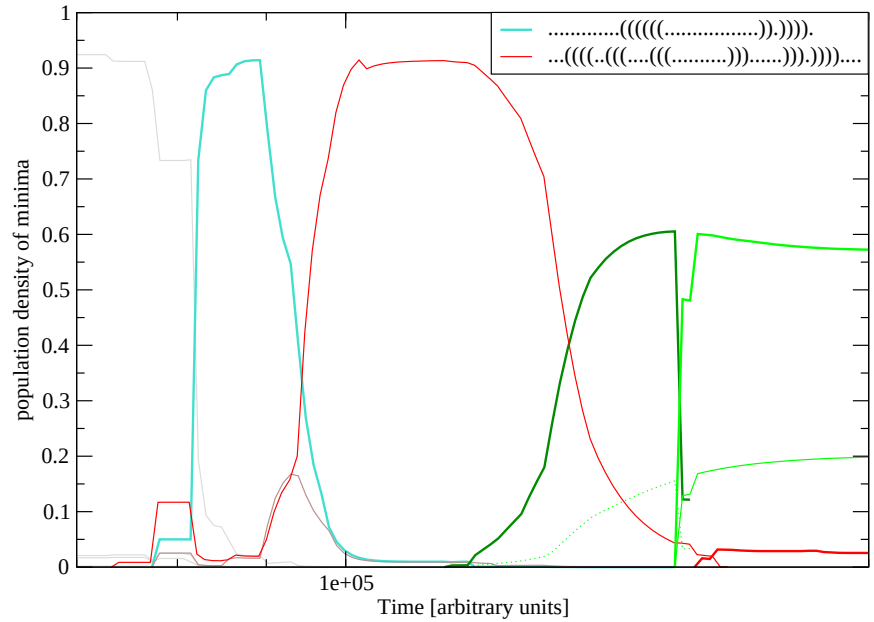


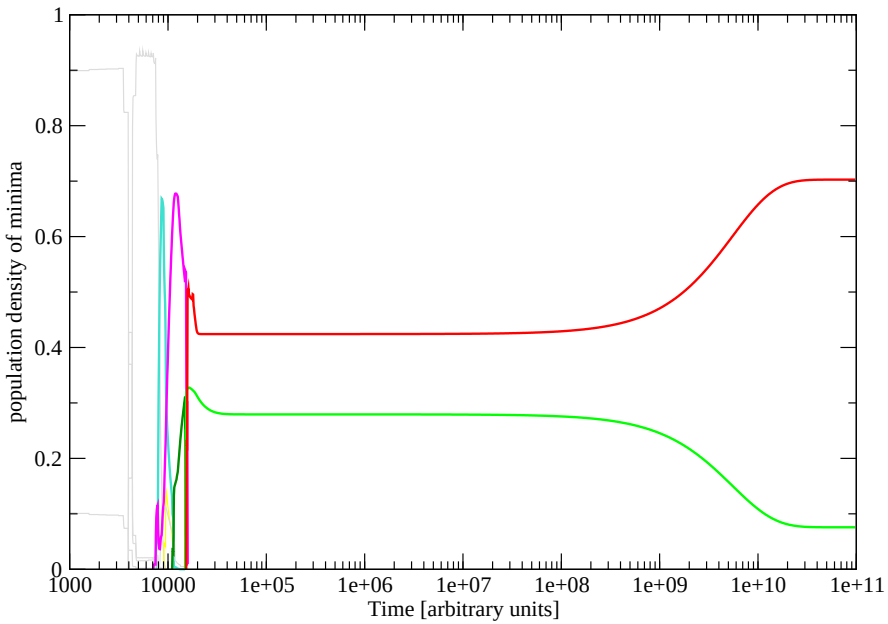
Melting a pore through RNA

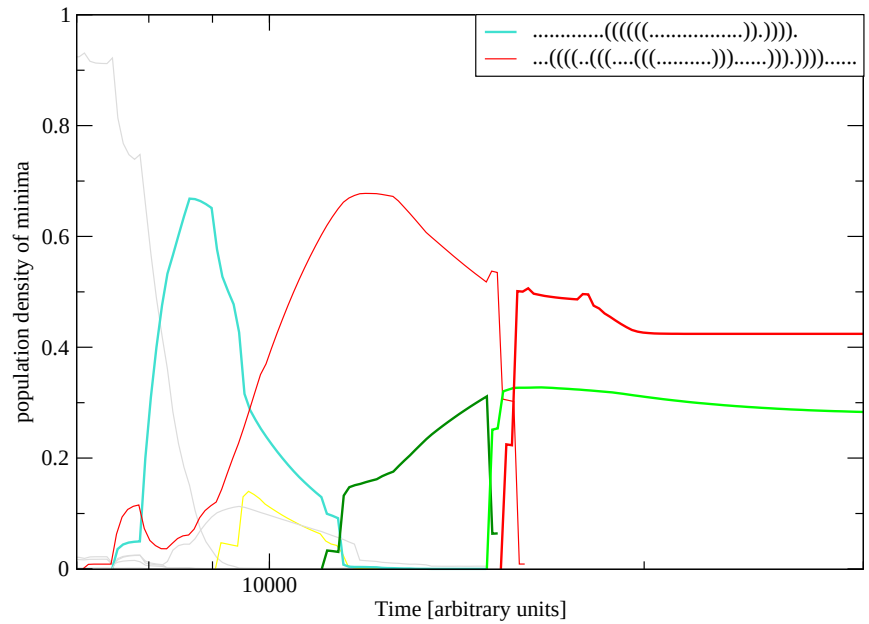


Transciption attenuation: phe-AAS from *E. coli*









- Kinetic simulations on varying energy landscapes are possible.
- Far from simulating the “natural” state of affairs.
- Design and/or engineering of these processes is a future goal.

Acknowledgments

Ivo Hofacker
Peter Stadler
Michael Wolfinger