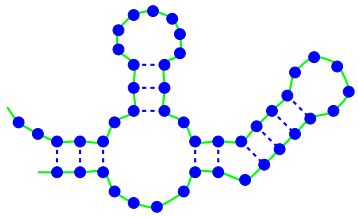
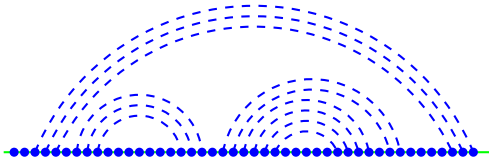
Statistical Mechanics of RNA Folding

R. Bundschuh, K. Hamacher, and T. Hwa
DAAD UC San Diego Beckman foundation

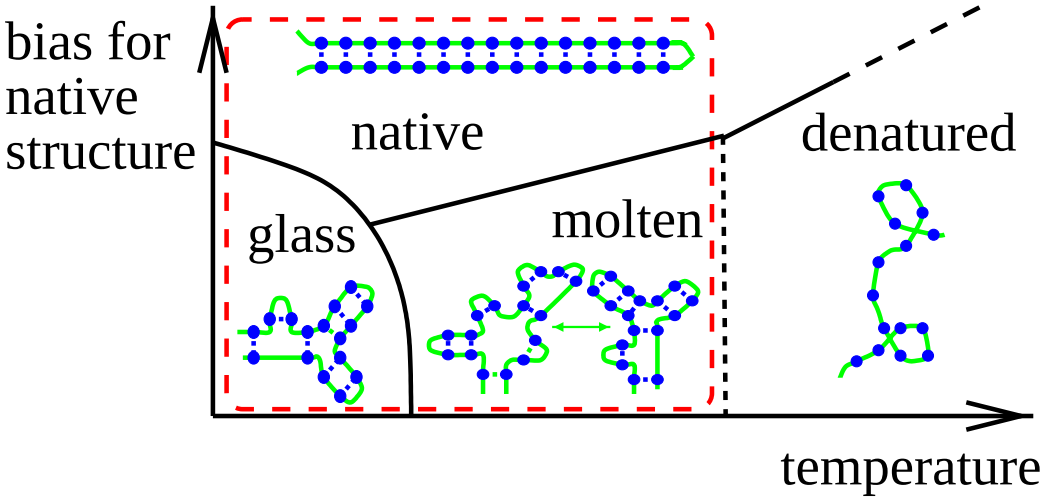
- RNA: single-stranded heteropolymer of A, U, C, G
- forms secondary structures by A–U and G–C base pairing



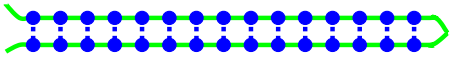
- tractable due to "Dyson" equation for its diagrammatic representation



- phase diagram similar to proteins



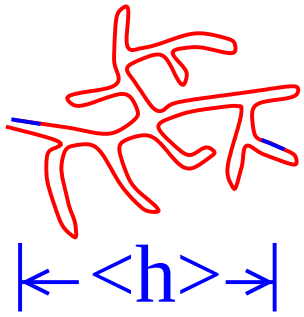
- suppress logarithmic loop entropy
- use long hairpin as native (designed) structure



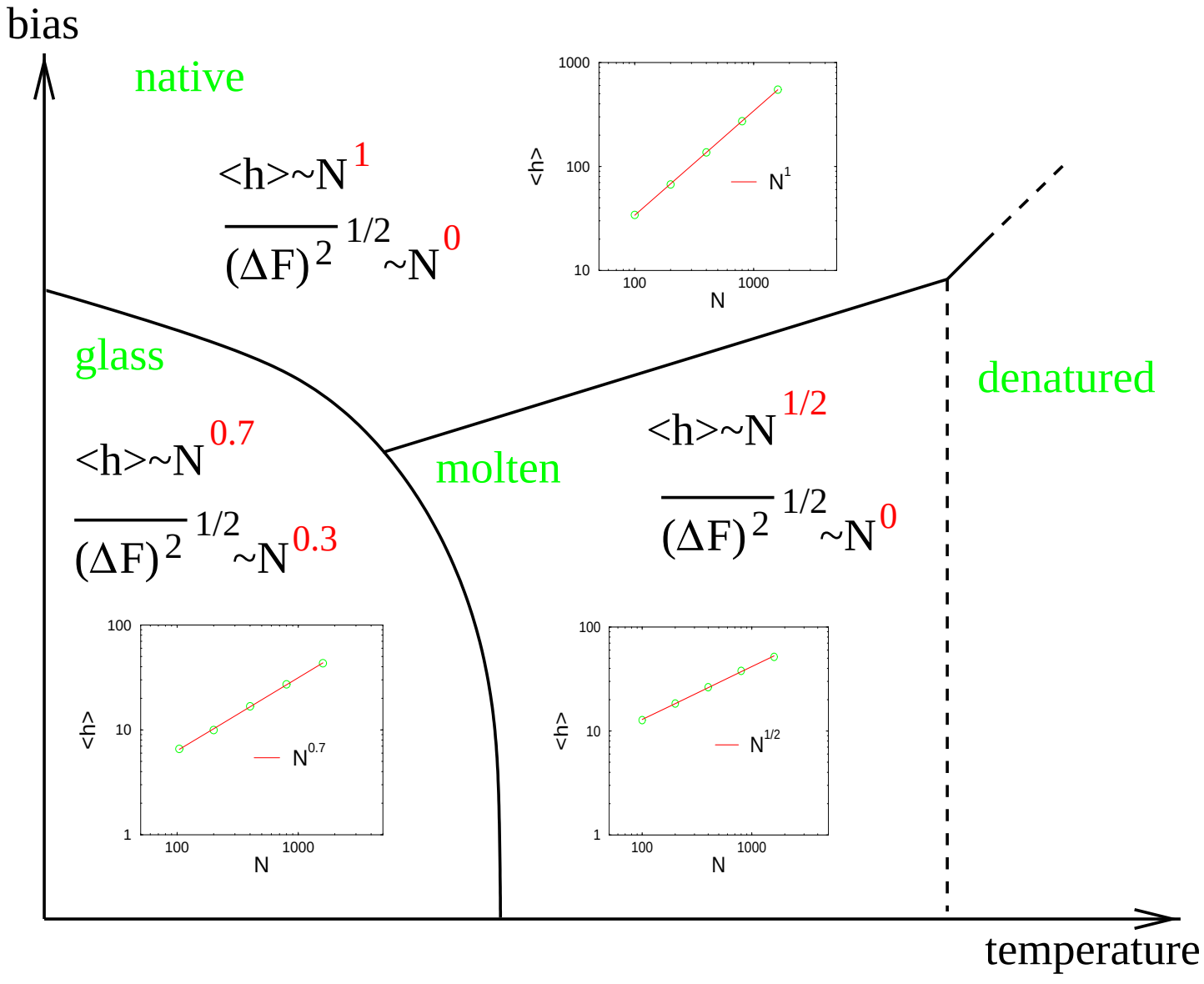
- create sequences by
  - randomly choosing first half of the sequence
  - assigning exact complement as second half
  - changing bias by mutations with probability p

Characterizing the Phases

- Characterization of the phases by scaling laws
- Quantities as a function of sequence length N
  - fluctuations of free energy $\overline{(\Delta F)^2}^{1/2}$
  - number of bonds $\langle h \rangle$ between first and middle base ("size of structure")



- Different scaling laws in all three phases:



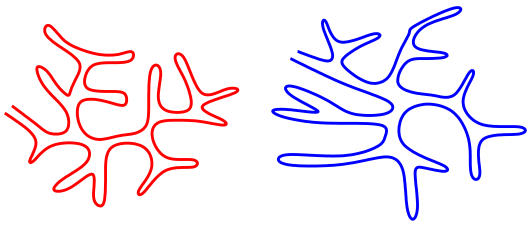
- Interaction energy between base i and base j

$$\varepsilon_{ij} = \varepsilon_0 + \Delta\varepsilon_{ij}$$

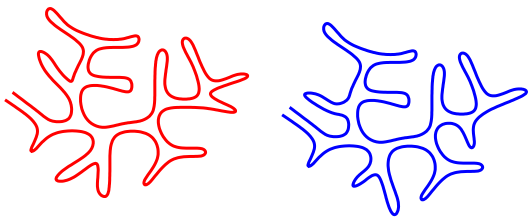
- Assume $\Delta\varepsilon_{ij}$ independent Gaussian variables

$$\overline{\Delta\varepsilon_{ij}} = 0 \qquad \overline{\Delta\varepsilon_{ij}\Delta\varepsilon_{kl}} = \Delta\epsilon\,\delta_{ik}\delta_{jl}$$

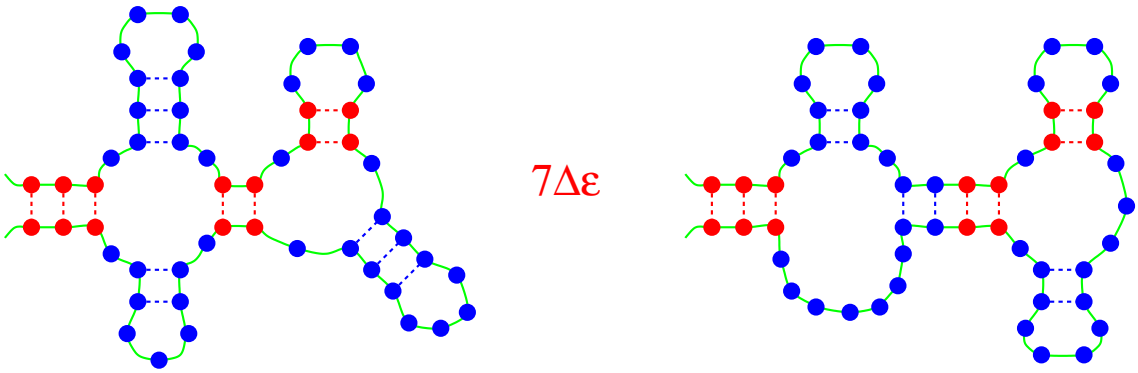
- Difference between glass and molten phase
  $\longrightarrow$ study two non interacting replicas with same disorder
  - $\Delta\varepsilon$ small
    $\rightarrow$ disorder not important
    $\rightarrow$ replicas independent



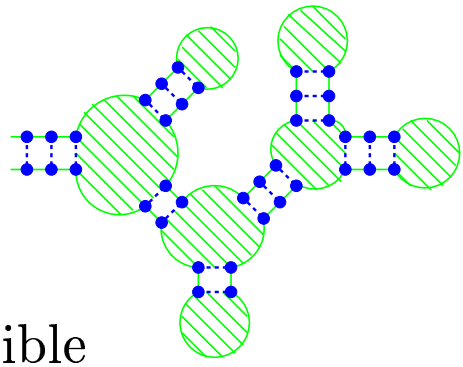
  - $\Delta\varepsilon$ large
    $\rightarrow$ disorder important (glass)
    $\rightarrow$ replicas locked together

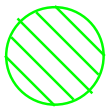


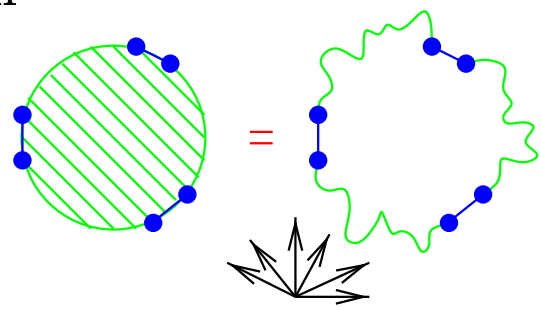
- ensemble average $\overline{Z^2}$ $\longrightarrow$ two replicas which gain energy $\Delta\varepsilon$ for every common bond (●┈┈●)



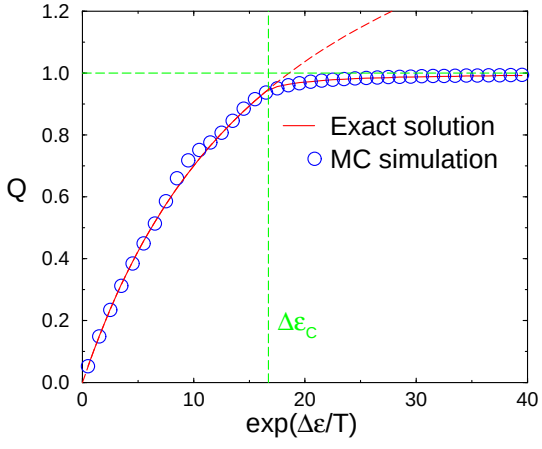
- Order configurations of 2 replica system by configurations of common bonds



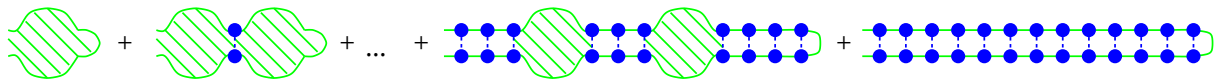
- Common bonds (●┄┄●) form RNA structure themselves
-  represents sum over all possible choices of non-common bonds in the two replicas
- 1 replica $\longrightarrow \ell^{-3/2} \Rightarrow$ 2 replicas $\longrightarrow (\ell^{-3/2})^2 = \ell^{-6/2}$
- effective picture: single RNA with "6-dimensional" loop entropies



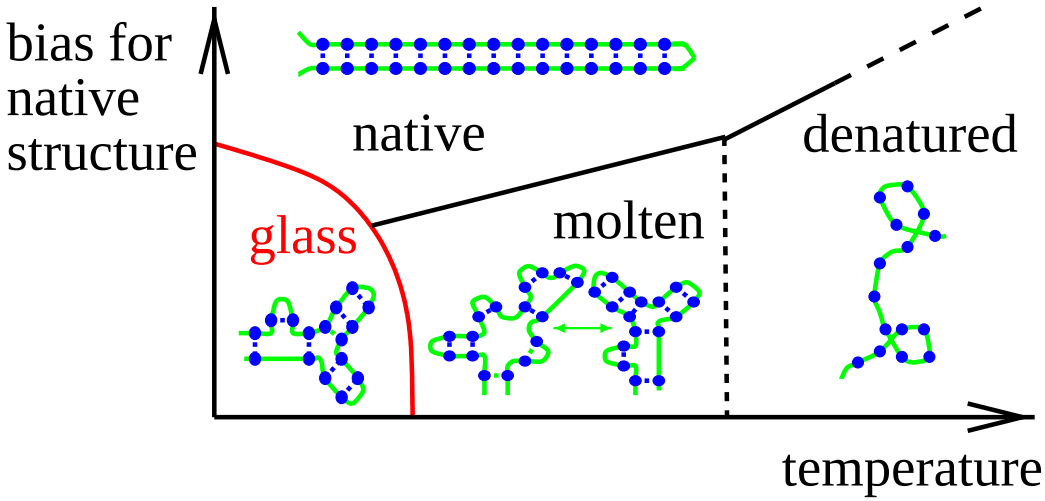
- exactly solvable
- phase transition at finite $\Delta\varepsilon_c$
  - $\Delta\varepsilon < \Delta\varepsilon_c$: 2 replicas fluctuate independently (molten
  - $\Delta\varepsilon > \Delta\varepsilon_c$: 2 replicas have same configuration (glass)
  - specific heat exponent $\alpha = 1$
    $\longrightarrow$ marginally first order transition
- fraction of common contacts



- order arbitrary structure by number of native contacts



-  = sum over all ways to place non-native bonds
- Folding from molten phase:
  exact solution (RB and TH, cond-mat/9903089)
- Folding from glass phase:
  scaling theory with glass phase scaling exponents
  $\longrightarrow$ second order transition with $\nu \approx 2.0$
- Glass phase and its phase transitions can be treated by means of statistical mechanics
- Work in progress:
  - whole phase diagram for 2 replica system
  - beyond 2 replicas
  - more realistic RNA model



- Glass phase and its phase transitions can be treated by means of statistical mechanics
- Work in progress:
  - whole phase diagram for 2 replica system
  - beyond 2 replicas
  - more realistic RNA model