Energy barriers in a pseudoknot conformation space

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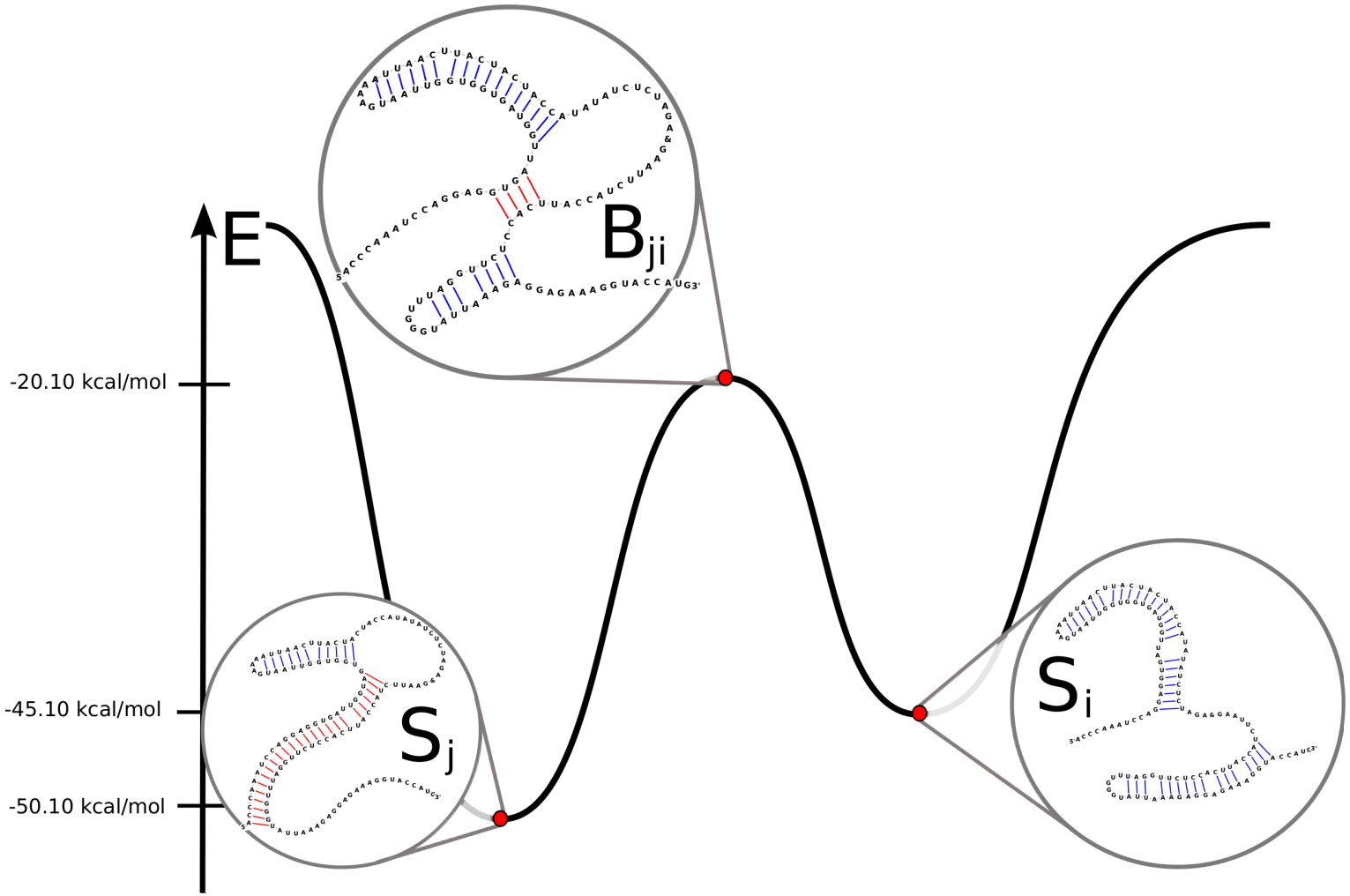
February 18, 2011

barrier heights



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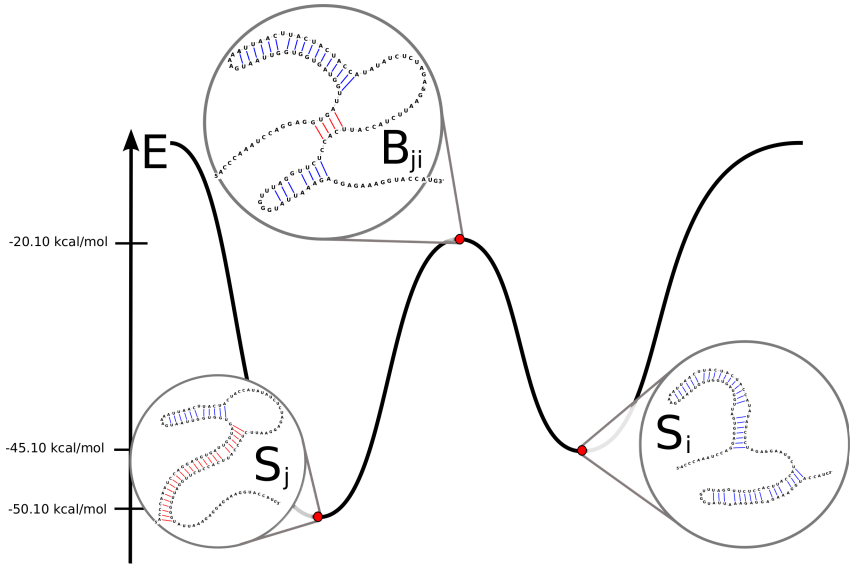
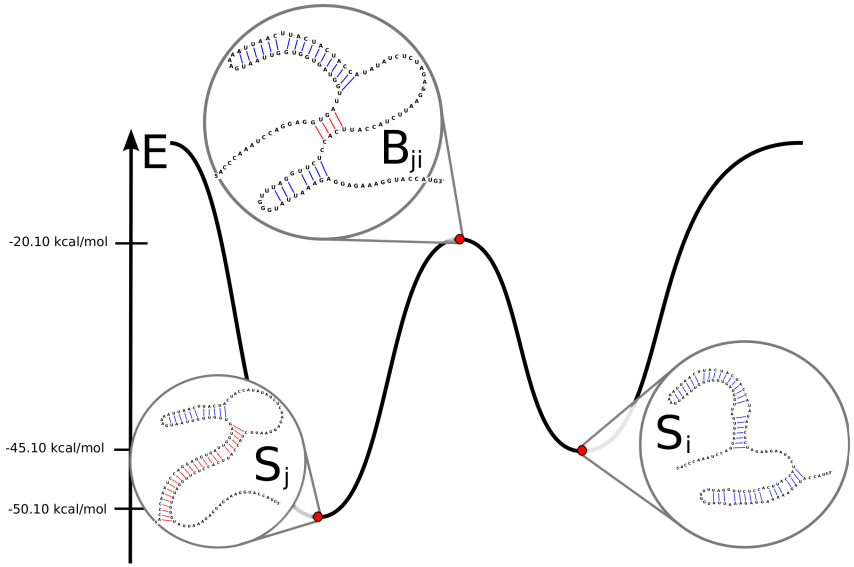


- Related problems
  - $\Rightarrow$ estimation of mfe importance

barrier heights



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  - $\Rightarrow$ estimation of mfe importance
  - $\Rightarrow$ cotranscriptional folding

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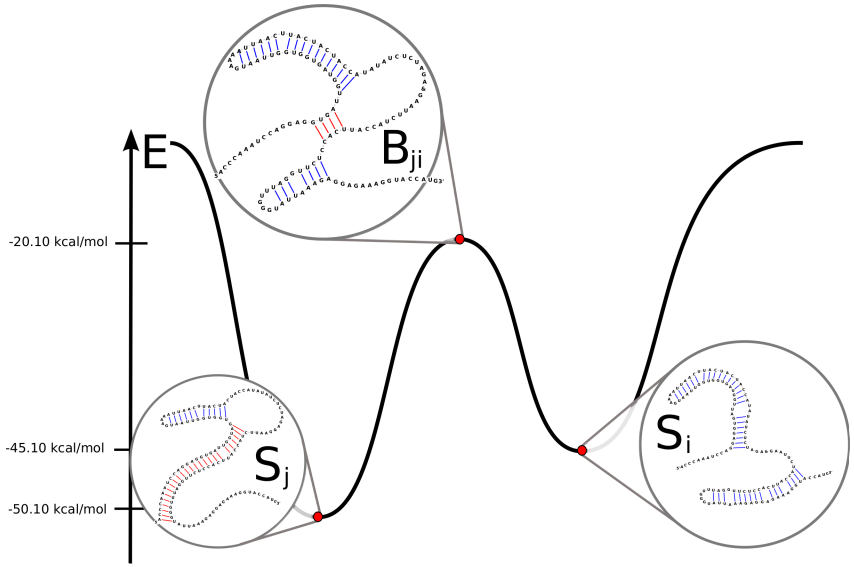

- Related problems
  - ⇒ estimation of mfe importance
  - ⇒ cotranscriptional folding
  - ⇒ switch design

efficient barrier computation

- standard computation
  - RNAsubopt including barrier structure
  - coarse graining: local minima, saddle points ($\Rightarrow$ barrier trees)

efficient barrier computation

- standard computation
  - RNAsubopt including barrier structure
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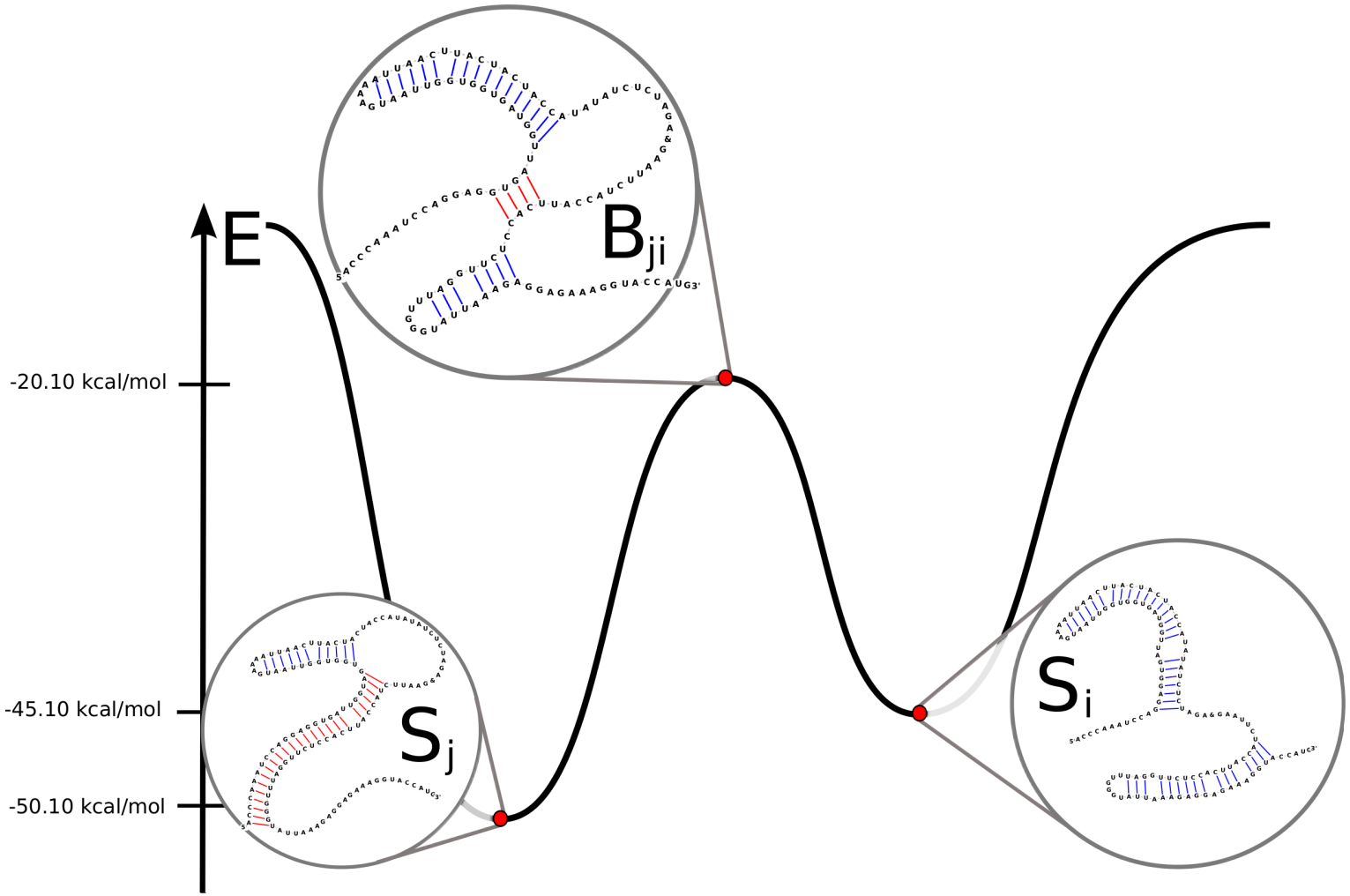
- problems
  - high barriers need big ΔE
  - subopt output increases with length of sequence

conventional vs. pseudoknot space



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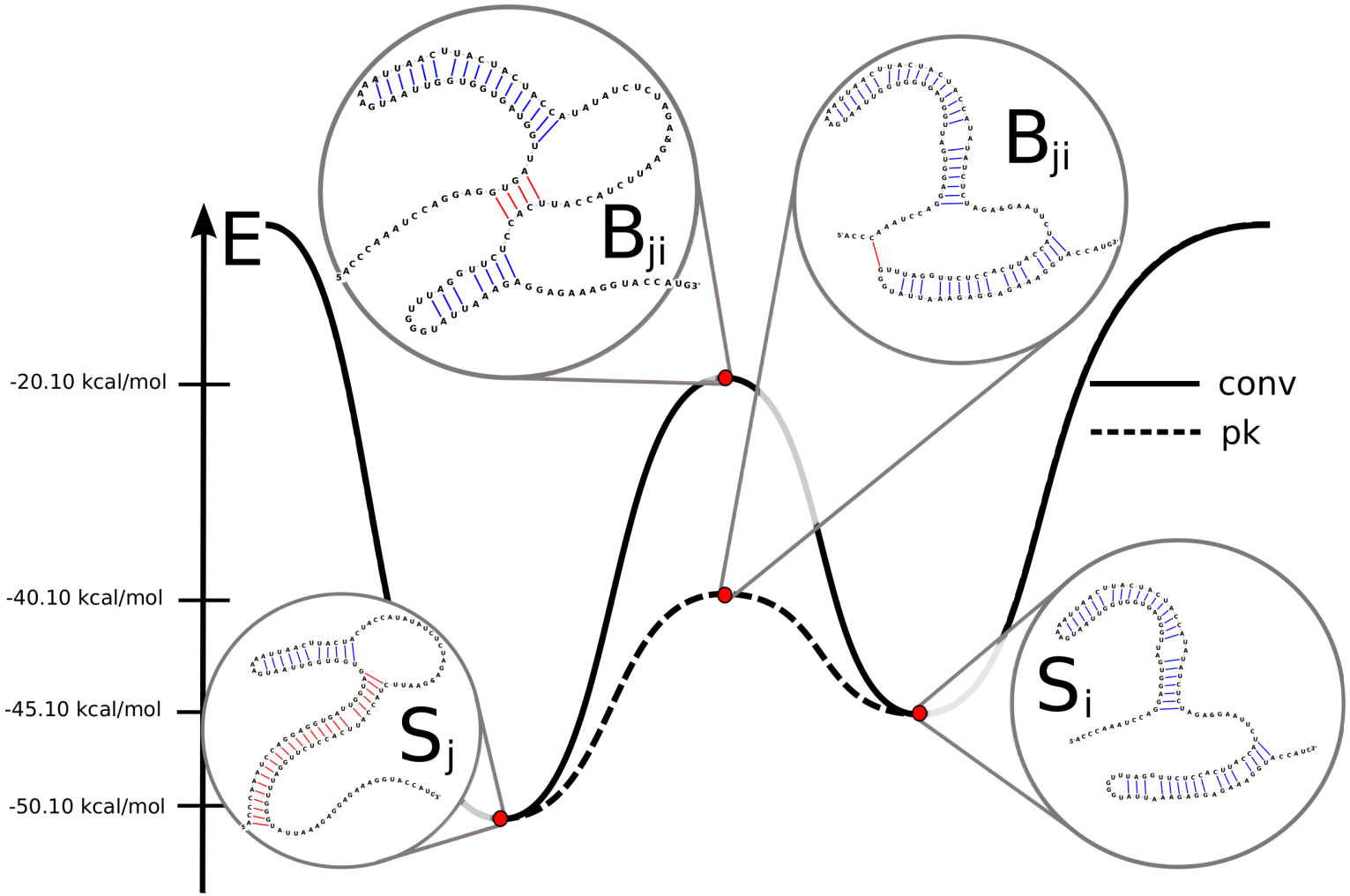


heuristics for pseudoknot space

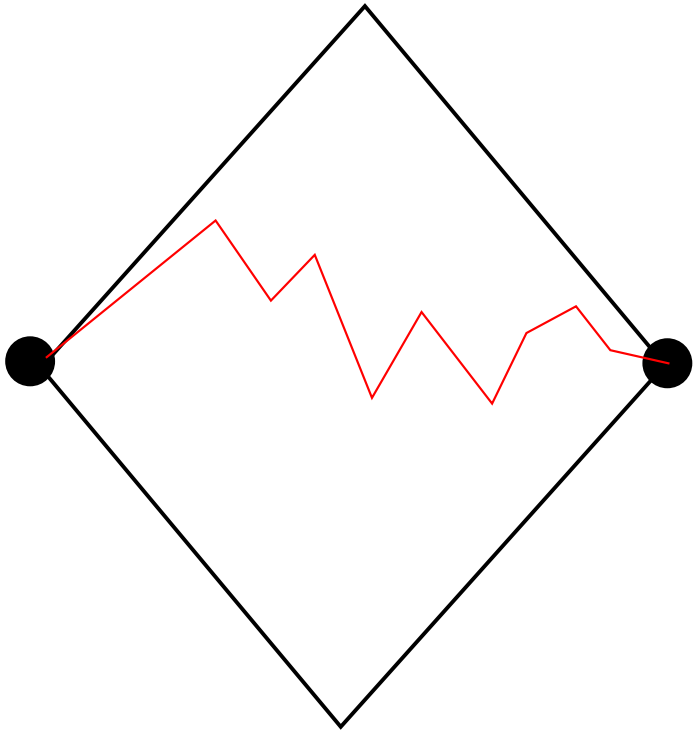
- Two heuristics
  - $\Rightarrow$ pk-findpath

heuristics for pseudoknot space

- Two heuristics
  - ⇒ pk-findpath
  - ⇒ guided (dirty) moveset

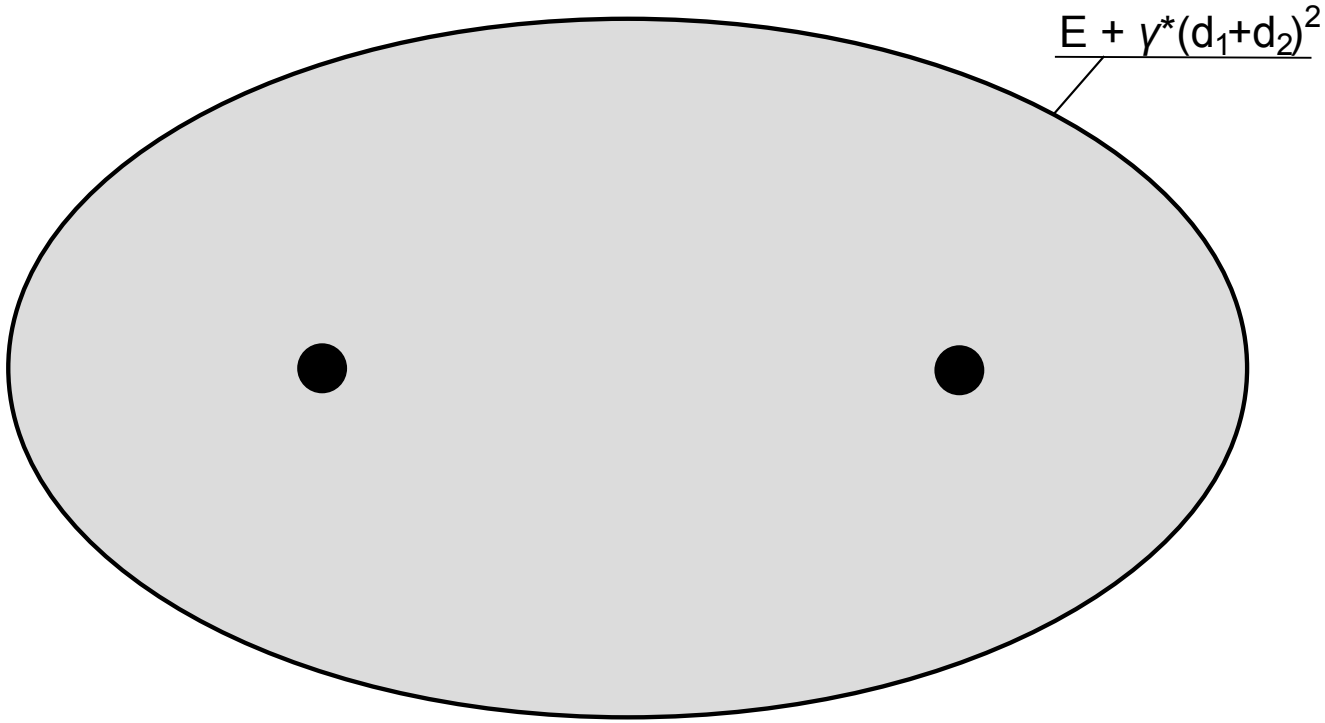
guided barrier detection

findpath, pk-findpath:



guided barrier detection

stacked helix moves in guided space:



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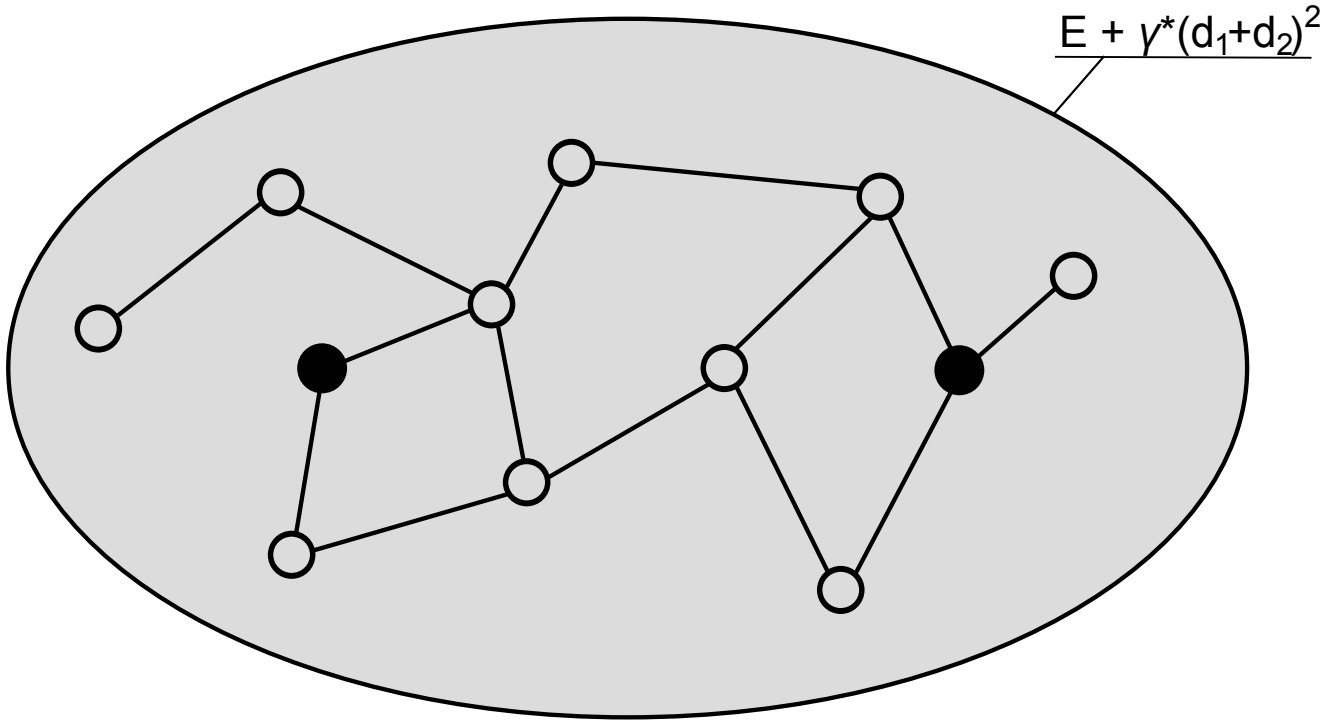

guided barrier detection

- set of structures G
- foreach structure in G
  apply moveset $\Rightarrow$ neighborhood N
- foreach structure in N
  find nearest local minimum and add to G if
  $E(S) + \gamma(d_1 + d_2)^2 \leq E(\text{pk-findpath}) + \gamma(d_{1,2})^2$

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  $E(S) + \gamma(d_1 + d_2)^2 \leq E(\text{pk-findpath}) + \gamma(d_{1,2})^2$
  - $\Rightarrow$ Extract shortest, energetically best path from network (bellman ford, ...)
  - $\Rightarrow$ Run treekin simulations to estimate first passage times

Thanks to: xtof, ivo, ronny and the tbi-crew

Thank you for your attention!