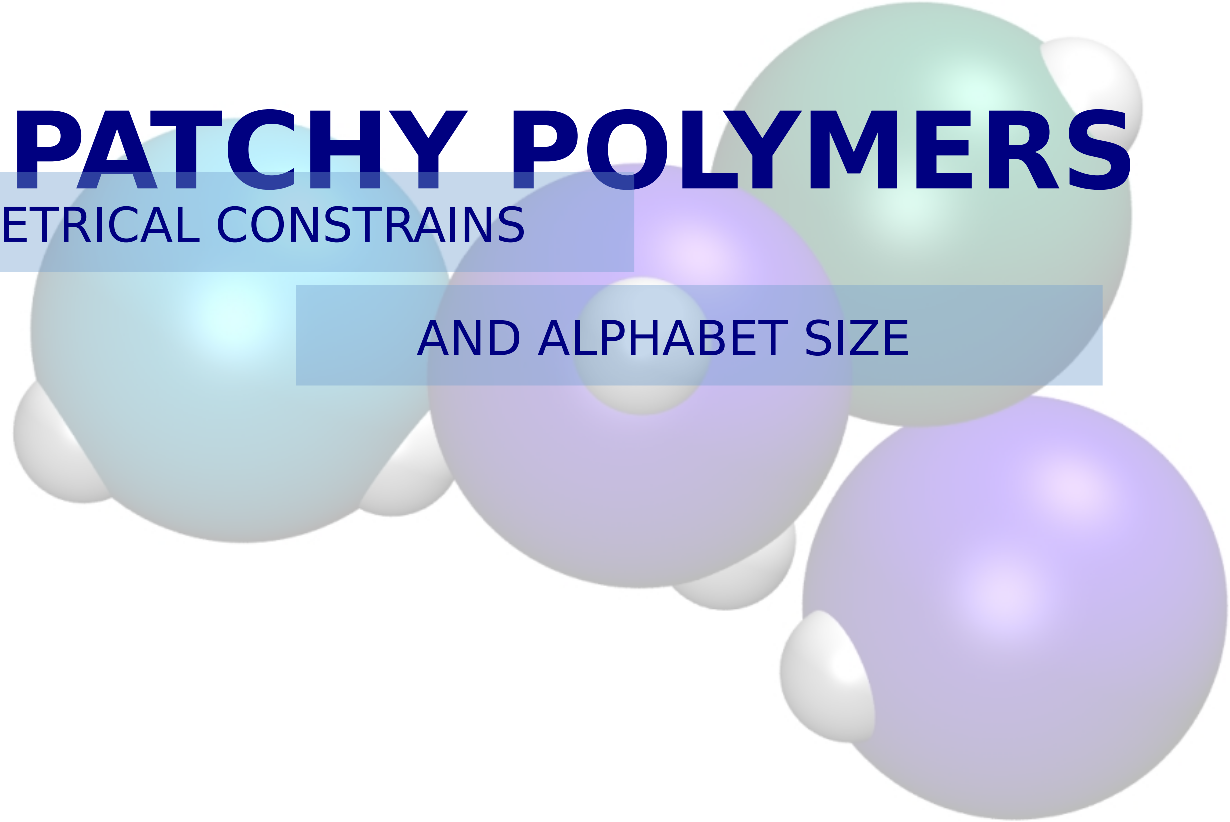
DESIGN OF PATCHY POLYMERS

INTERPLAY BETWEEN GEOMETRICAL CONSTRAINS

AND ALPHABET SIZE



Cardelli C., Coluzza I., Bianco V.,Computational Physics Group, Physics Department, University of Vienna

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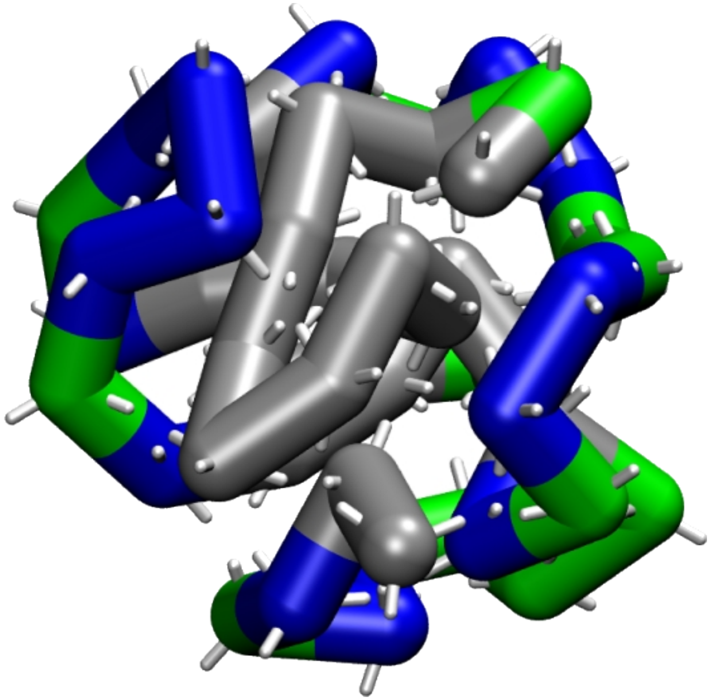
What allows different heteropolymers to fold?

Protein

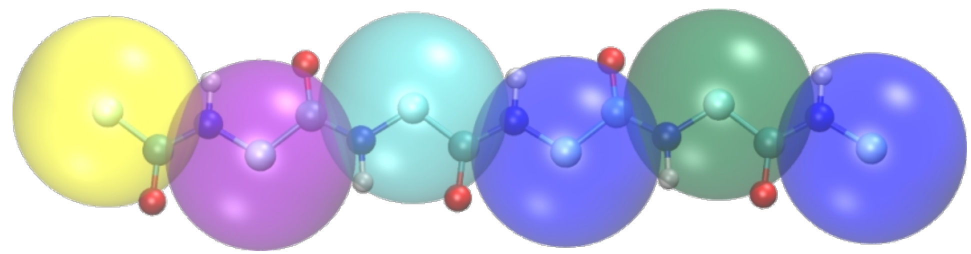


Patchy Polymer

What allows different heteropolymers to fold?

- Specific sequences fold into stable structures
- Made by 20 different types of amminoacids

Protein

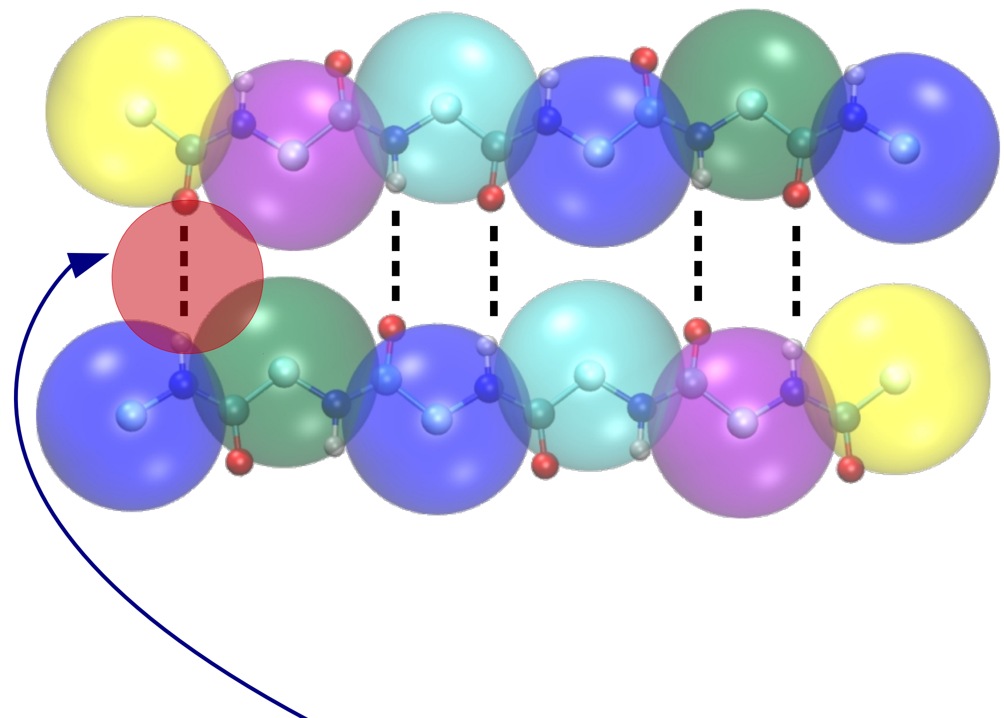


Specific sequence

What allows different heteropolymers to fold?

- Valence is the key to understand protein folding
- The system is designable if a minimum number of valence limiting interactions is included → reduce the configurational space of compact structures

Protein



Hydrogen Bonds

Coluzza, I., & Dellago, C. (2012).. *Journal of Physics: Condensed Matter*, *24*(28), 284111
Coluzza, I., Van Oostrum, P. D. J., Capone, B., Reimhult, E., & Dellago, C. (2013). Physical Review Letters, 110(7), 075501.
Coluzza, I., Van Oostrum, P. D. J., Capone, B., Reimhult, E., & Dellago, C. (2012). *Soft Matter*, *DOI*, 10.1039/2sm26967h.

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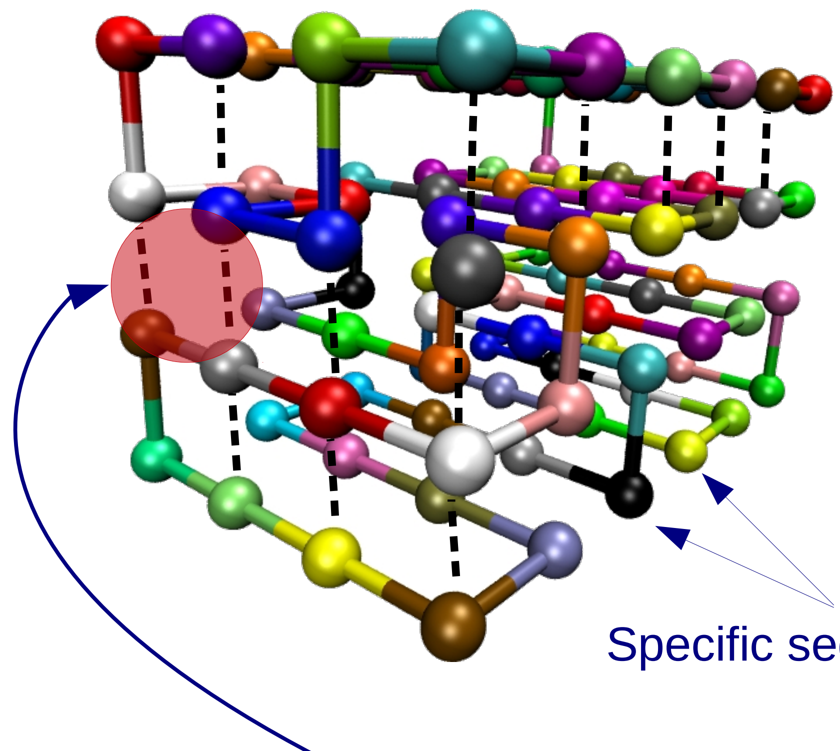
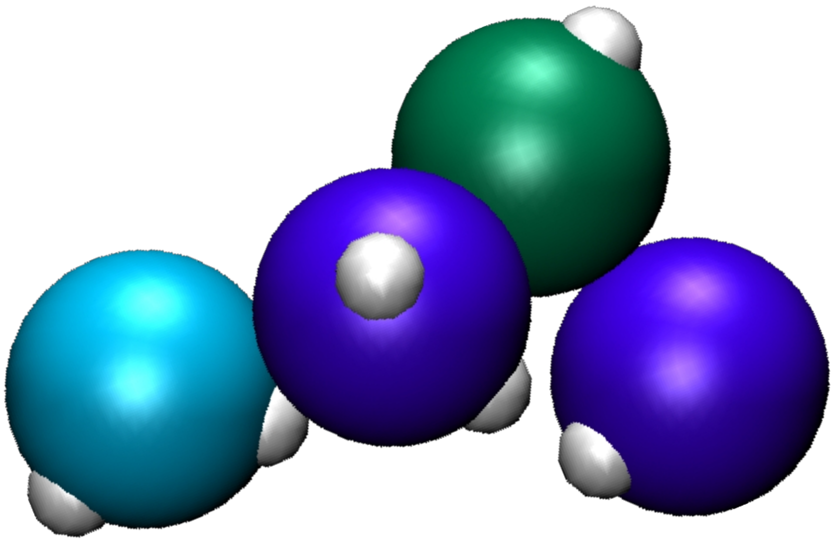
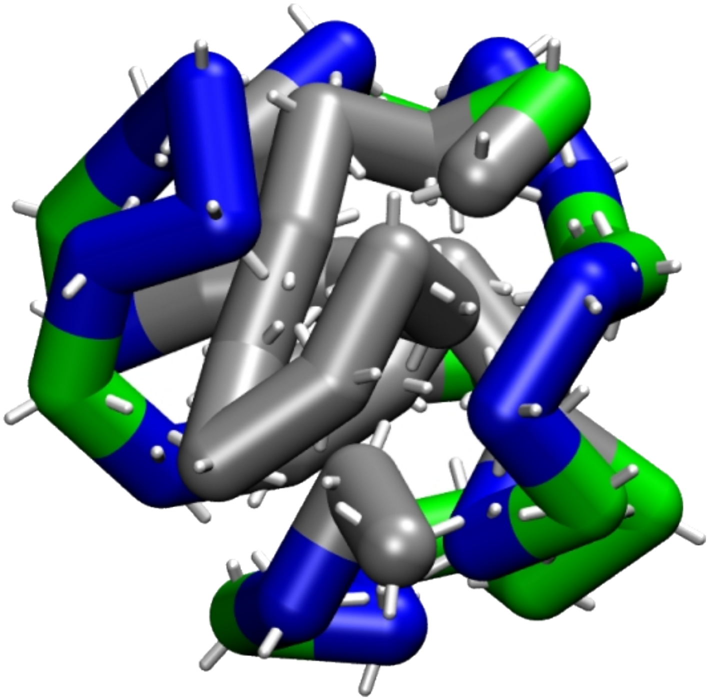


Protein model on lattice

Patchy Polymers as bionic proteins

- Following this principle we can copy protein design and folding into an artificial system

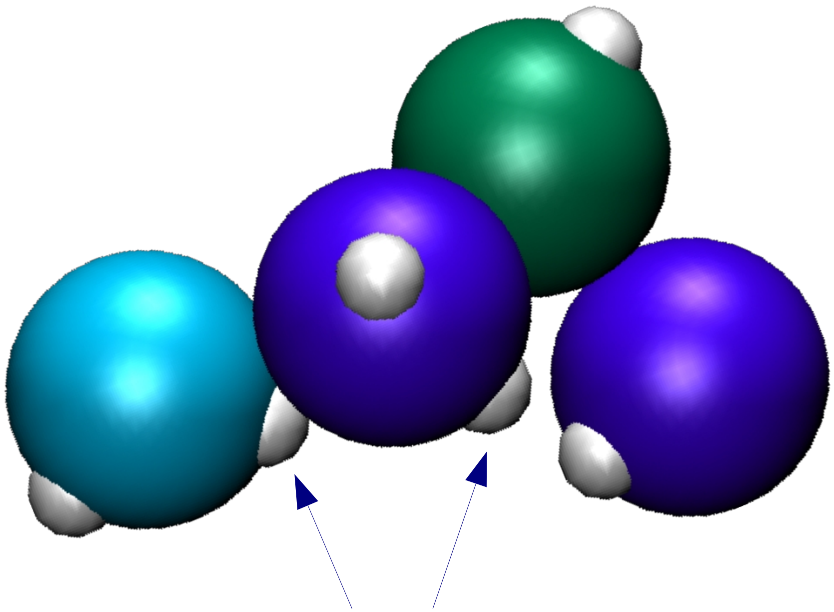




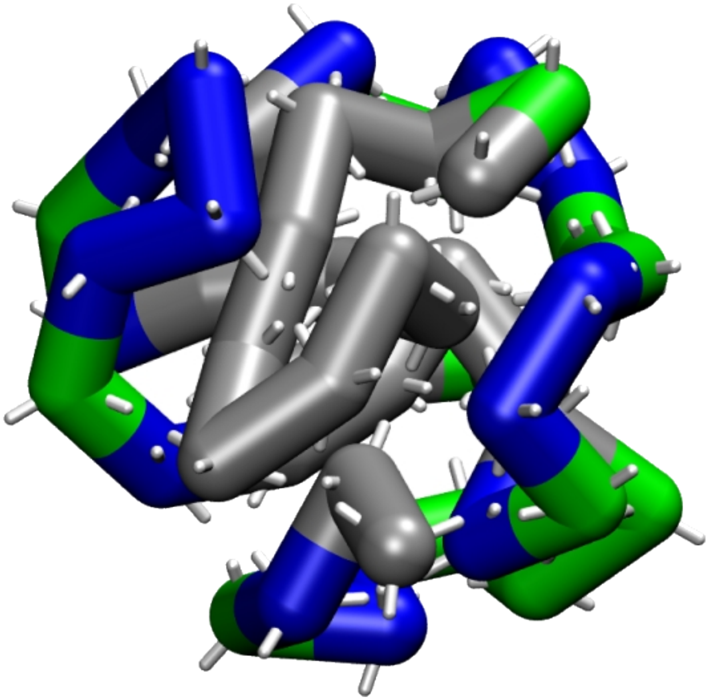
Patchy Polymer

Patchy Polymers as bionic proteins

- Following this principle we can copy protein design and folding into an artificial system
- Valence = directional interactions between the patches



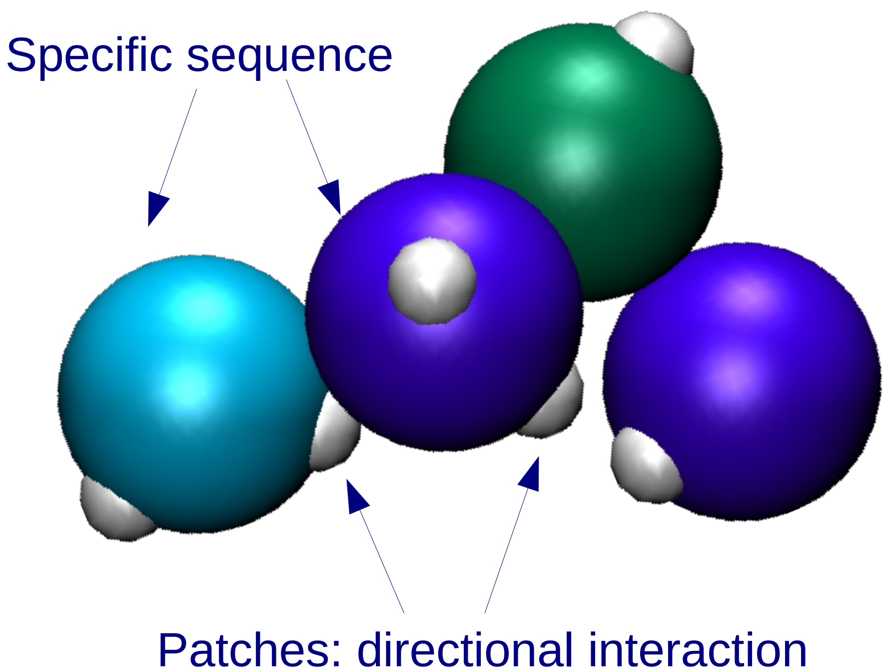
Patches: directional interaction

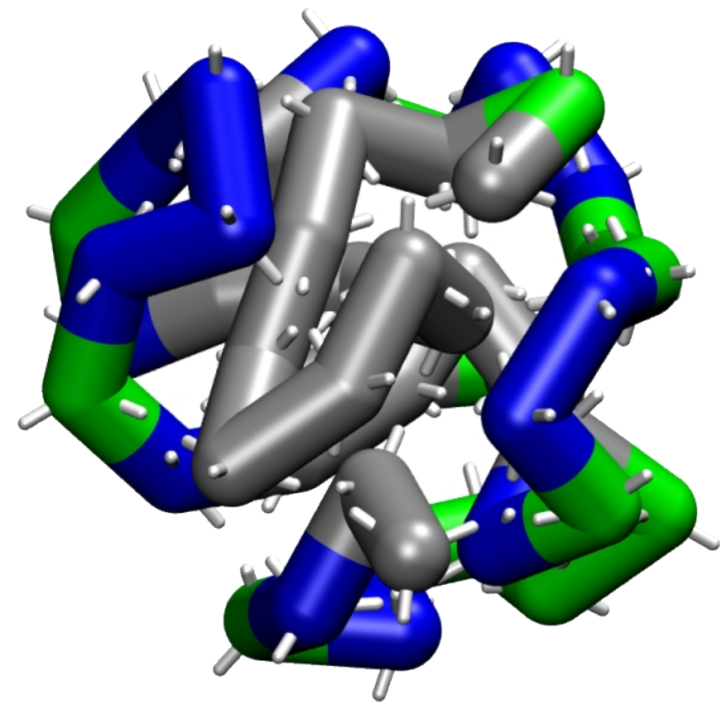


Patchy Polymer

Patchy Polymers as bionic proteins

- Following this principle we can copy protein design and folding into an artificial system
- Valence = directional interactions between the patches
- Specific sequence = alphabet of different isotropic interactions

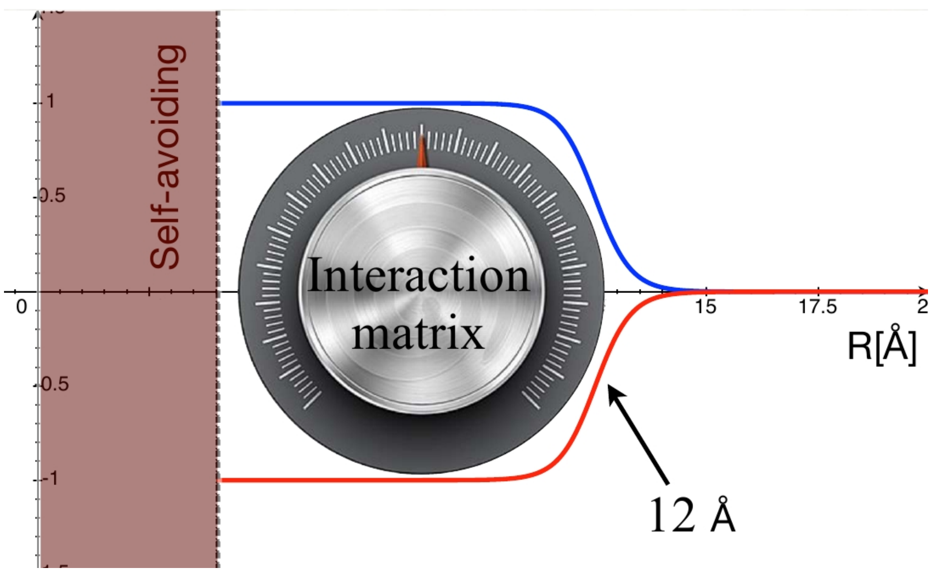


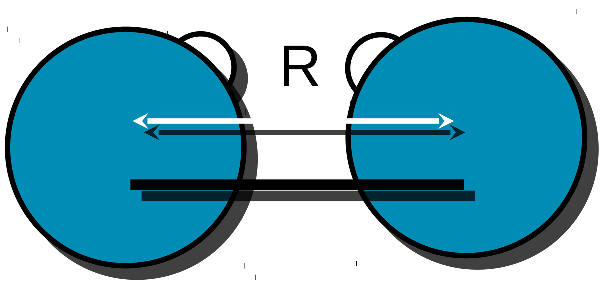


Patchy Polymer

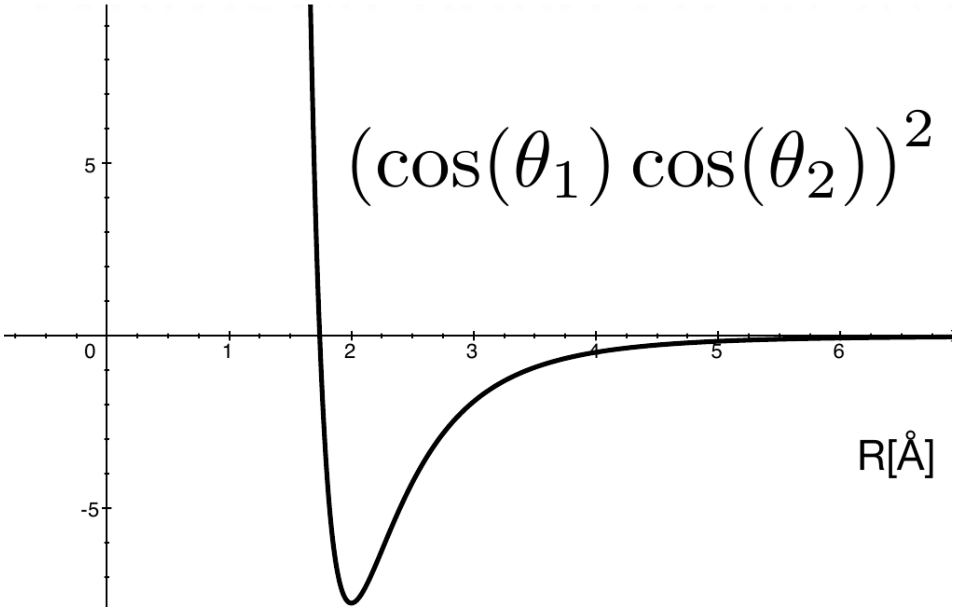
Patchy Polymers as bionic proteins

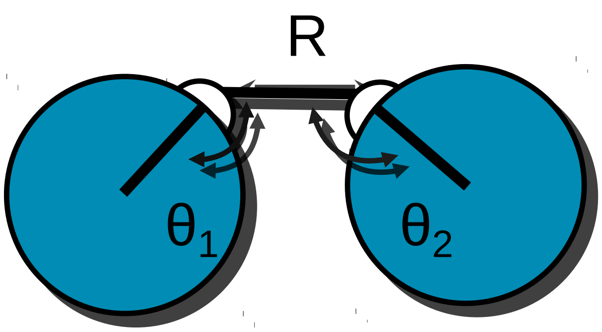
Isotropic interaction





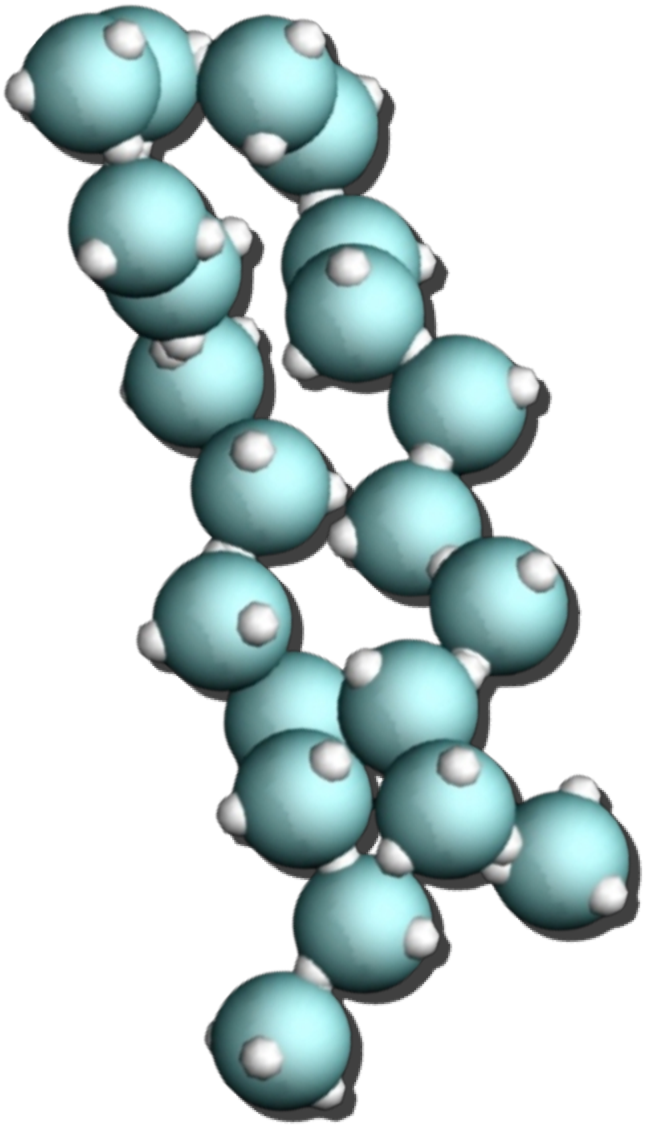
Directional interaction

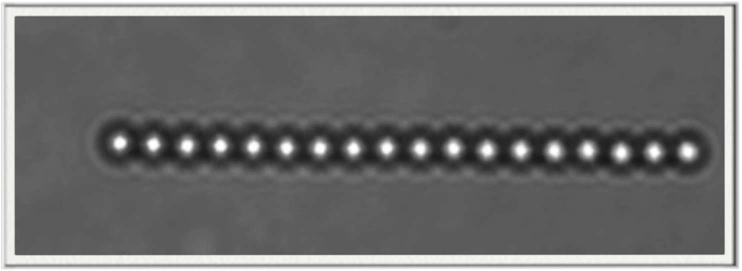




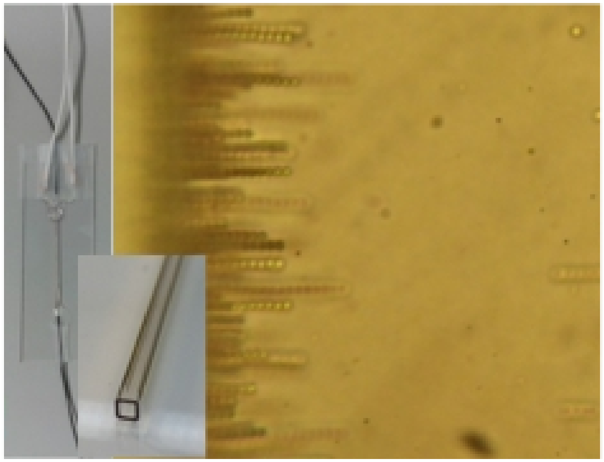
Patchy Polymers as bionic proteins

- Production of novel materials with specific self-assembly properties

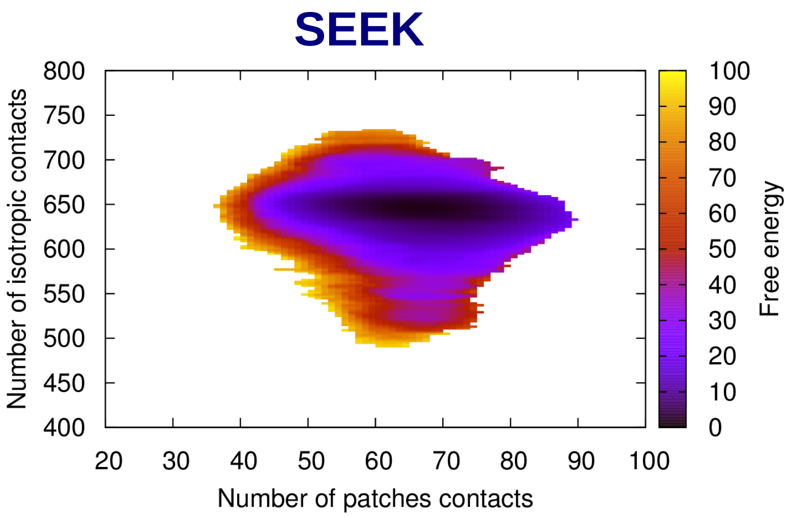




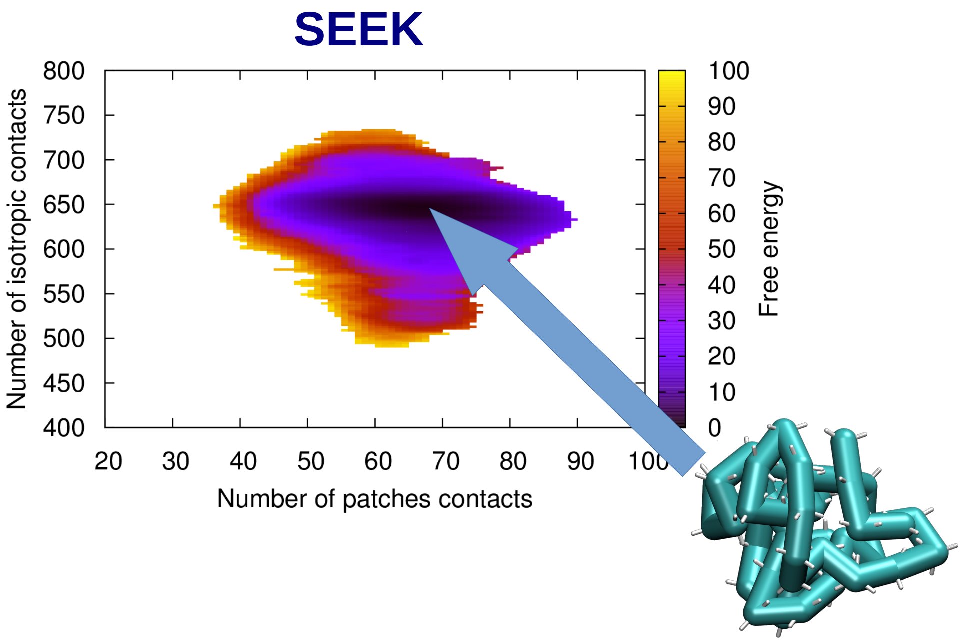
Peter van Oostrum et al. BOKU, Vienna Austria



Design and Folding of Patchy Polymers

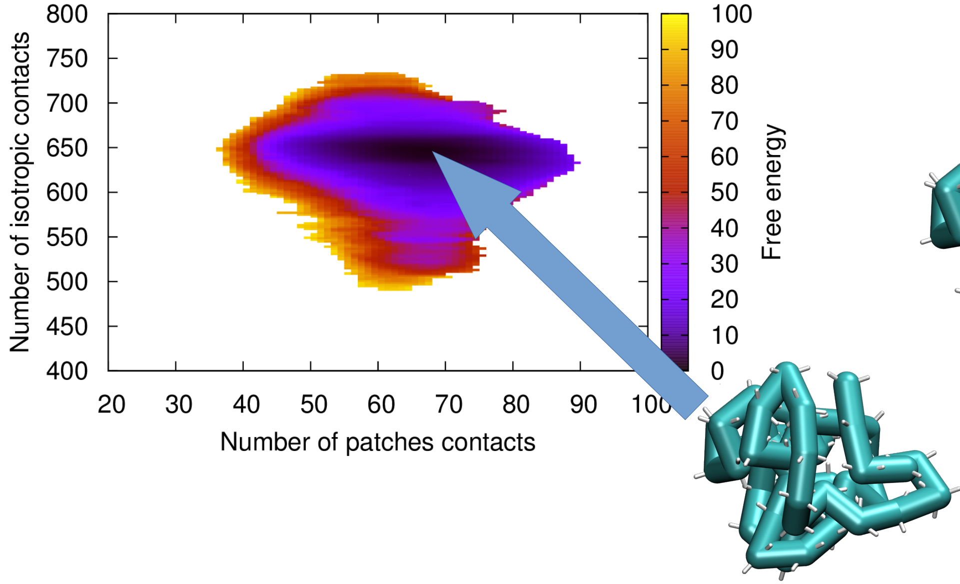


Design and Folding of Patchy Polymers

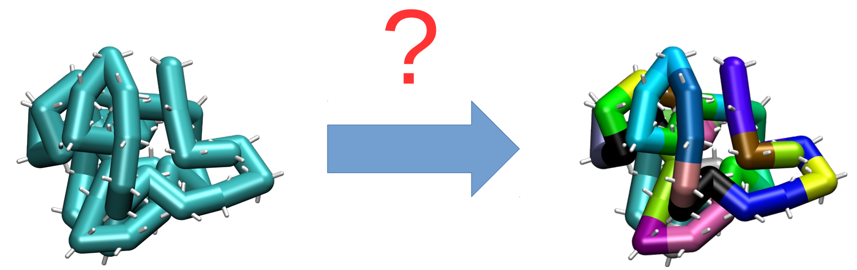


Design and Folding of Patchy Polymers

SEEK



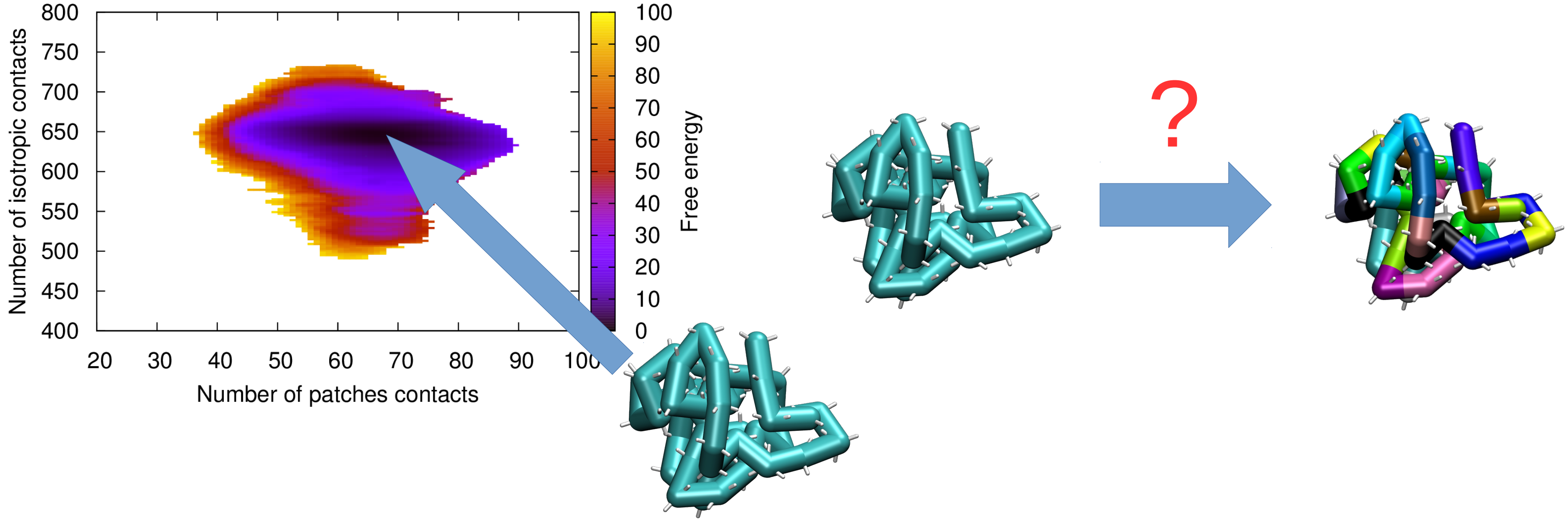
DESIGN

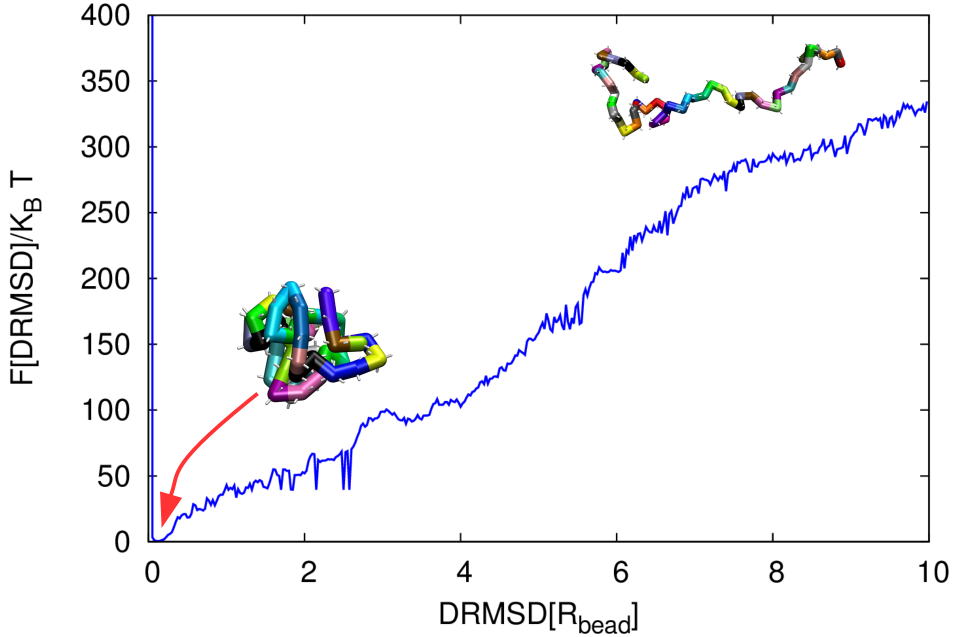


Design and Folding of Patchy Polymers

SEEK

DESIGN





FOLDING

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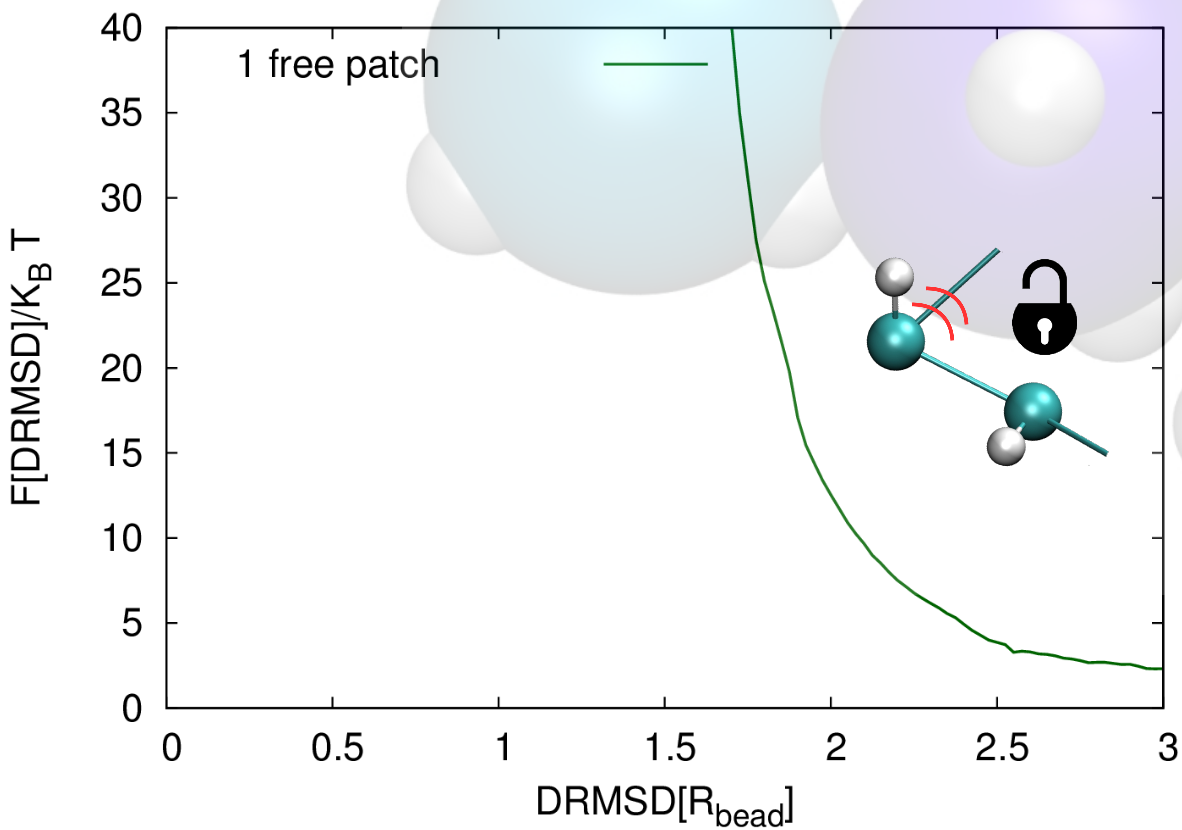
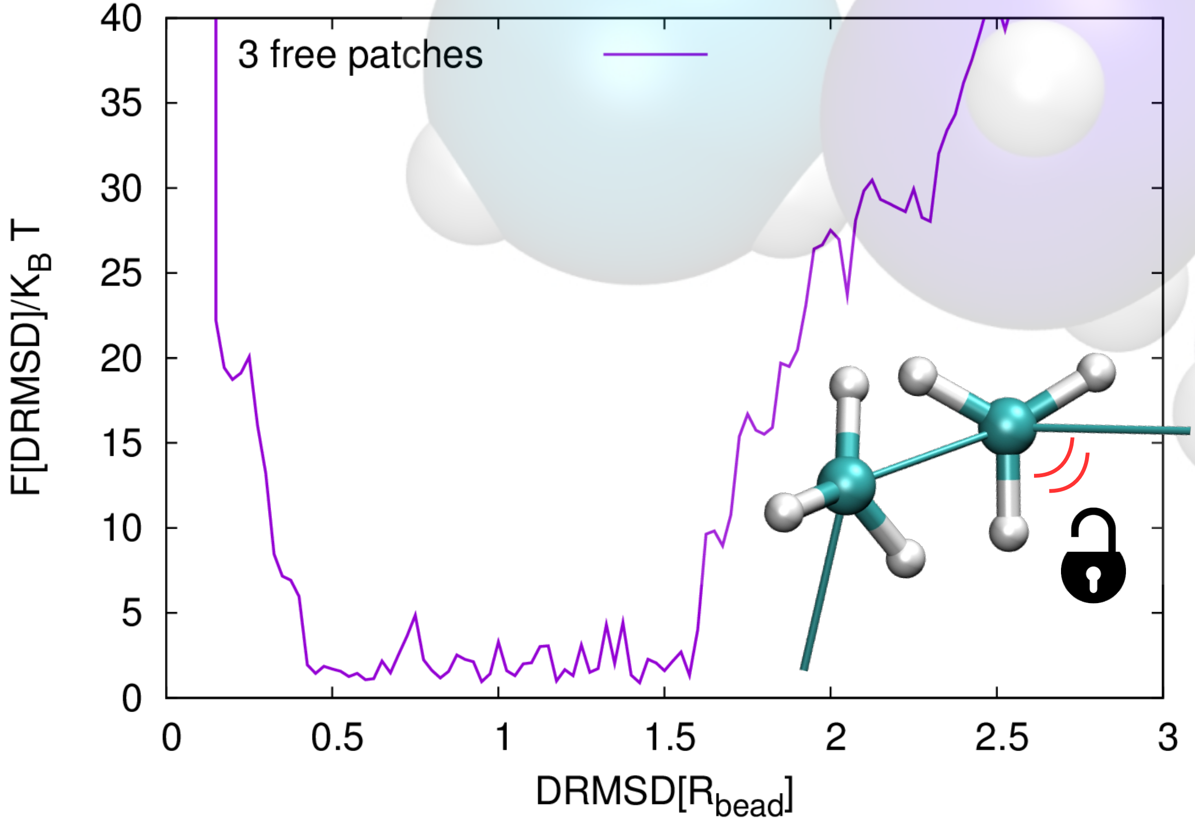
How does the folding depend on the number and the structure of the patches?



The 1 patch is free to rotate with respect to the backbone

Free energy landscape vs Distance Root Mean Square Displacement (DRMSD) for **one free patch** with alphabet size of 3.

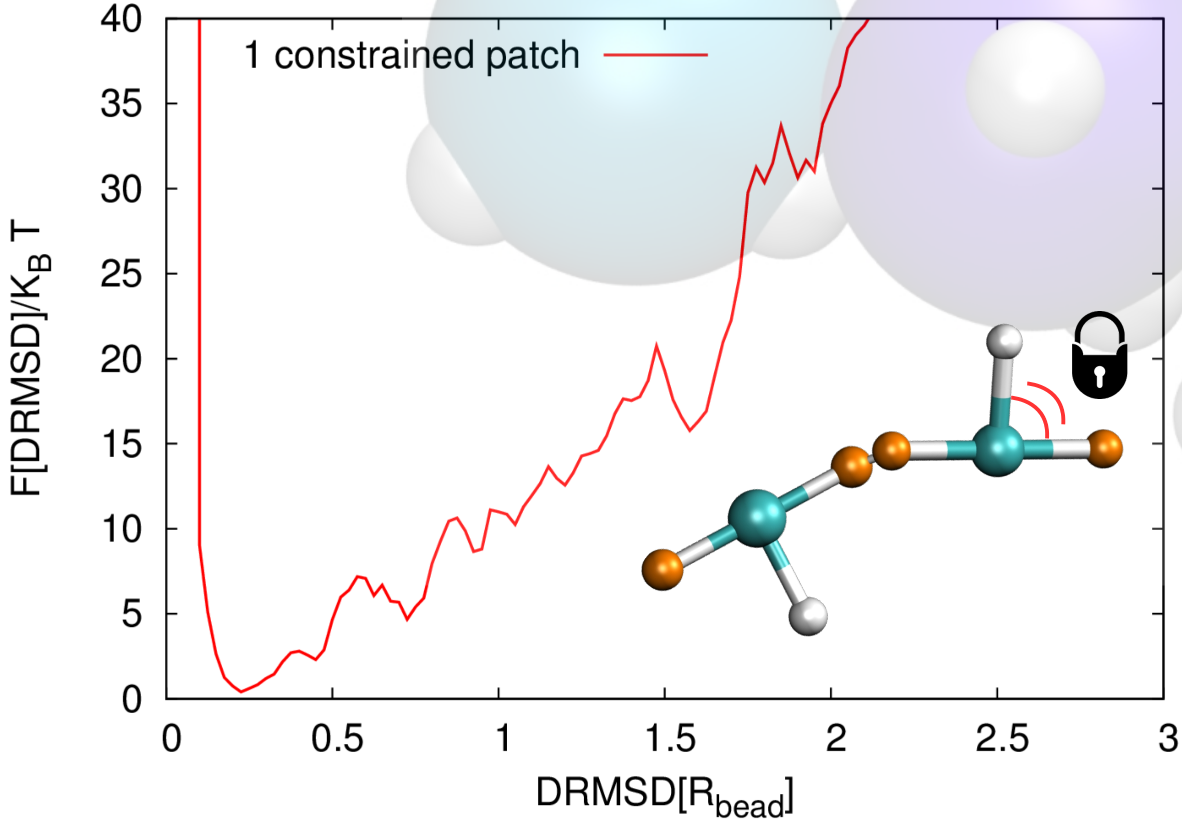
How does the folding depend on the number and the structure of the patches?



The 3 patches are free to rotate with respect to the backbone

Free energy landscape vs DRMSD for **3 free patches** with alphabet size of 3.

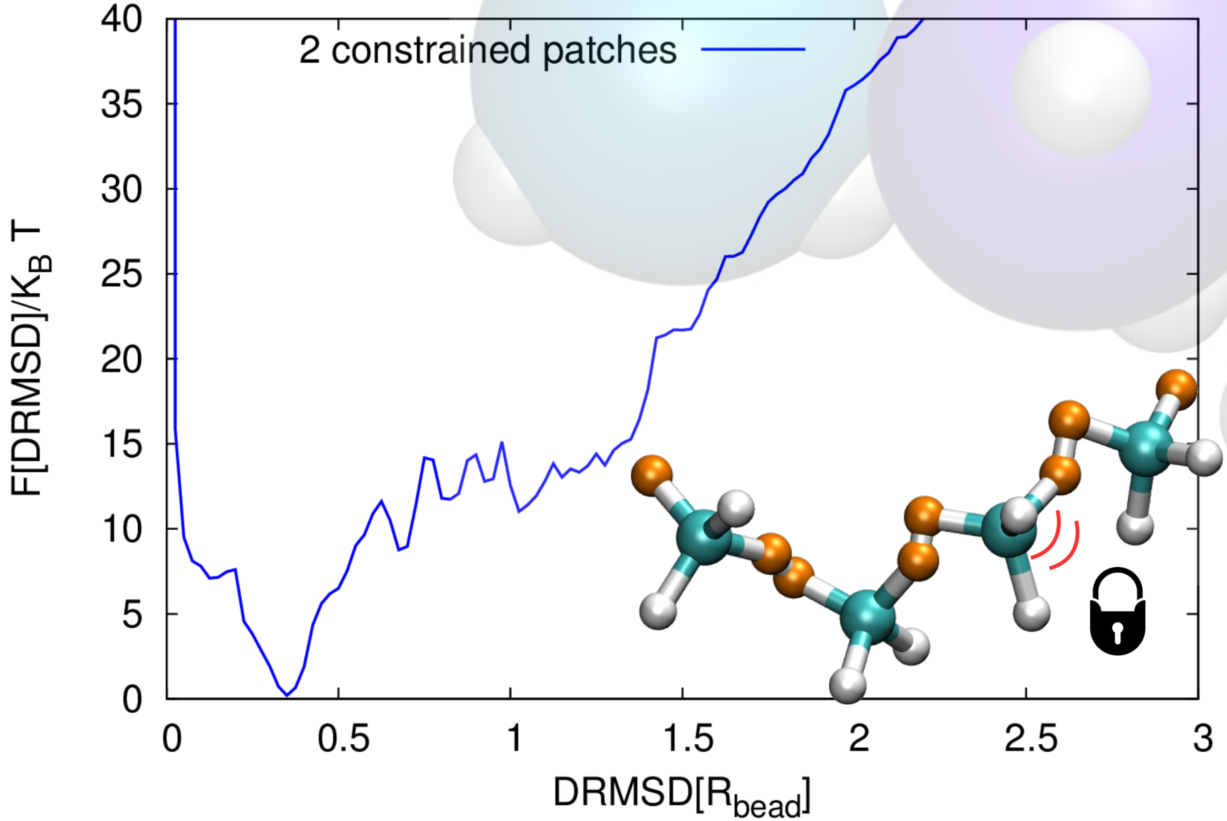
How does the folding depend on the number and the structure of the patches?



The 1 patch is constrained with respect to the backbone

Free energy landscape vs DRMSD for **one patch constrained to the backbone** with alphabet size of 3.

How does the folding depend on the number and the structure of the patches?



The 2 patches are constrained with respect to the backbone

Free energy landscape vs DRMSD for **2 patches constrained to the backbone** with alphabet size of 3.

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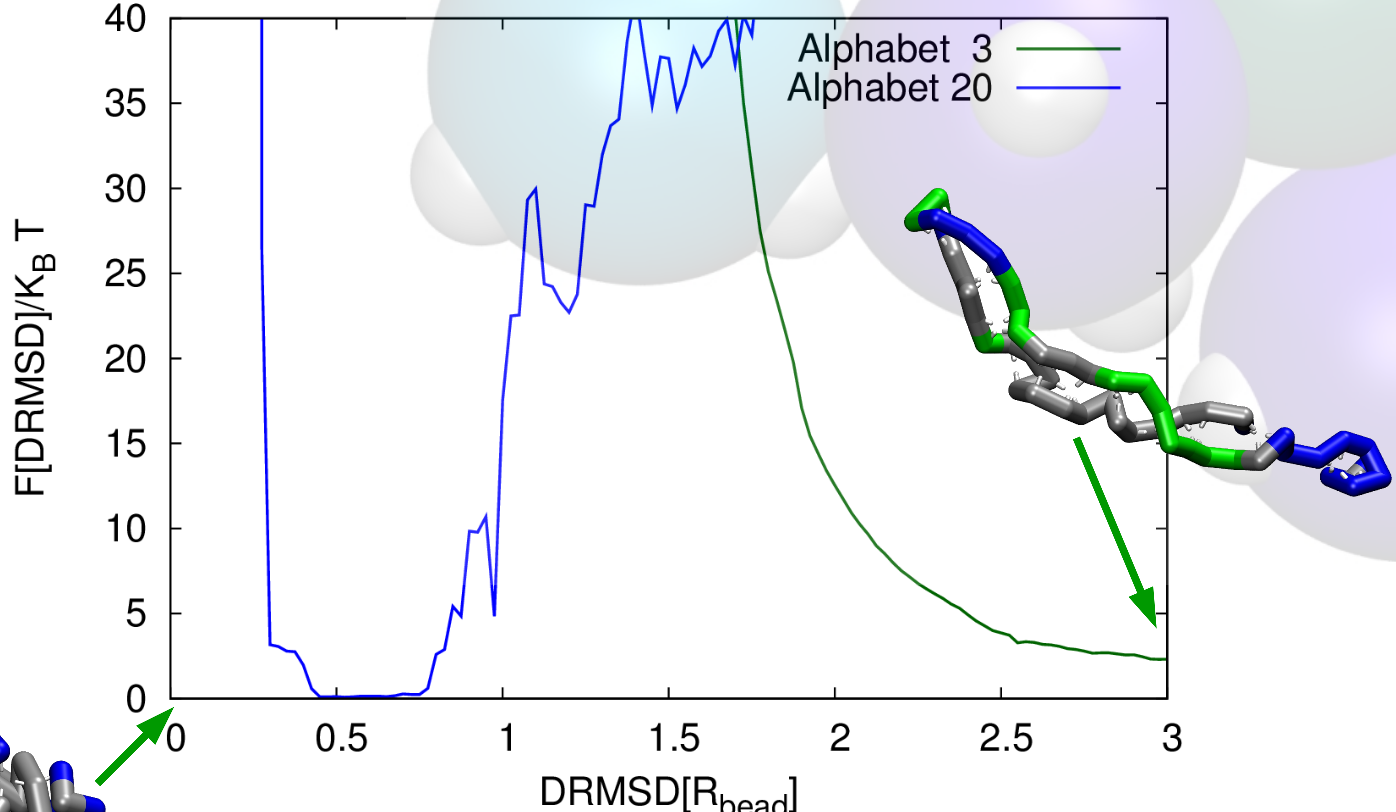
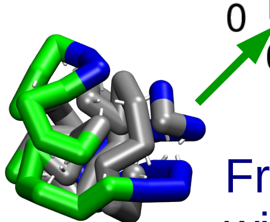
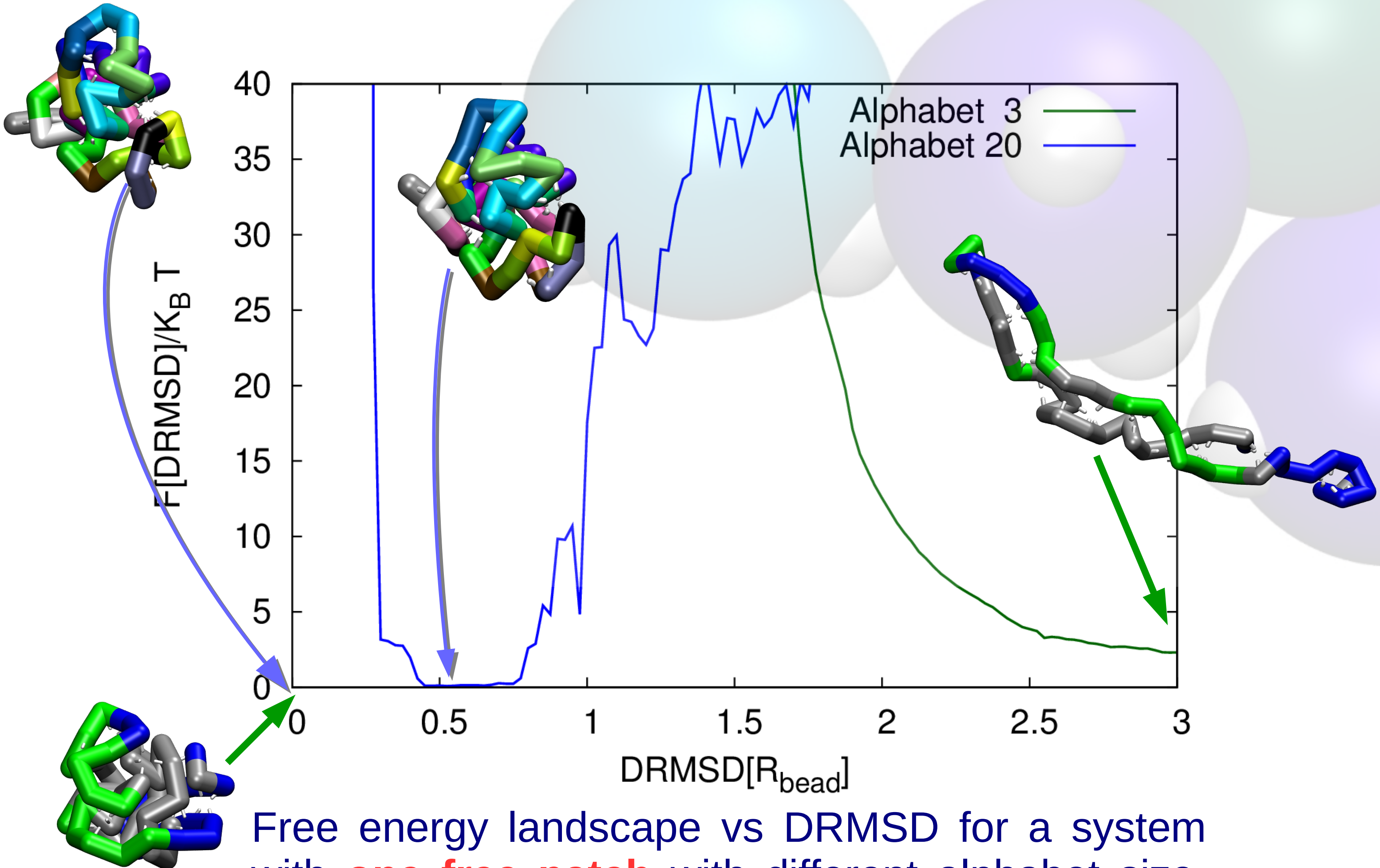
How does the folding depend on the alphabet size?





Free energy landscape vs DRMSD for a system with **one free patch** with different alphabet size. Only the sequence with alphabet size of 20 folds into the target structure.

How does the folding depend on the alphabet size?



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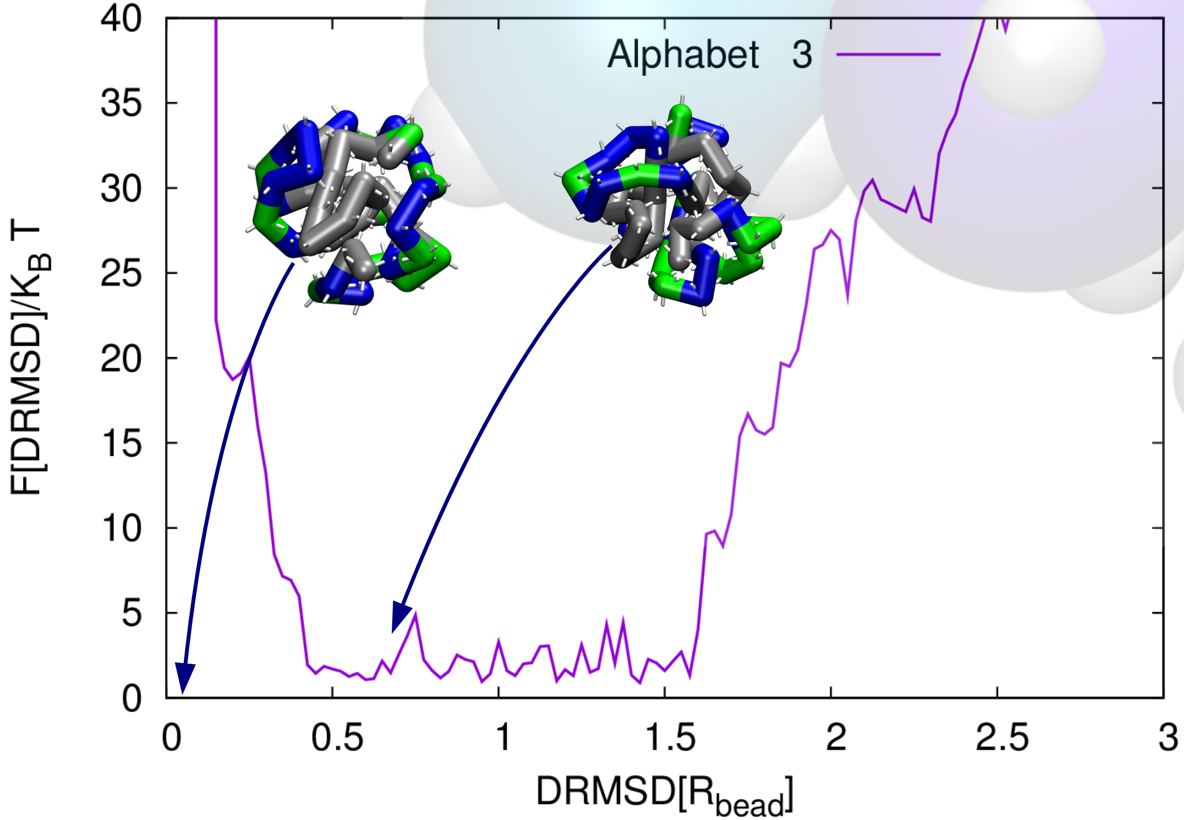
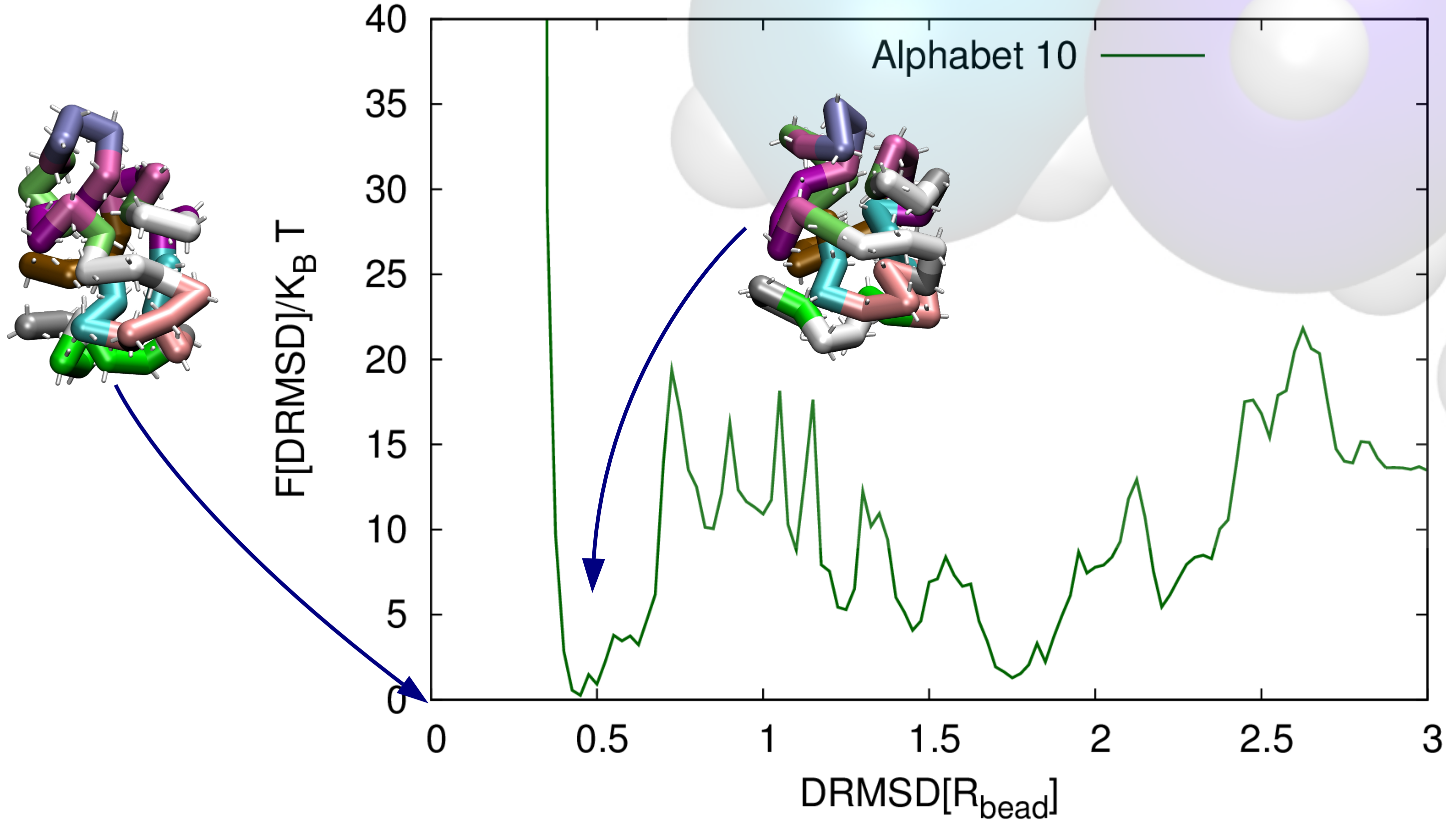


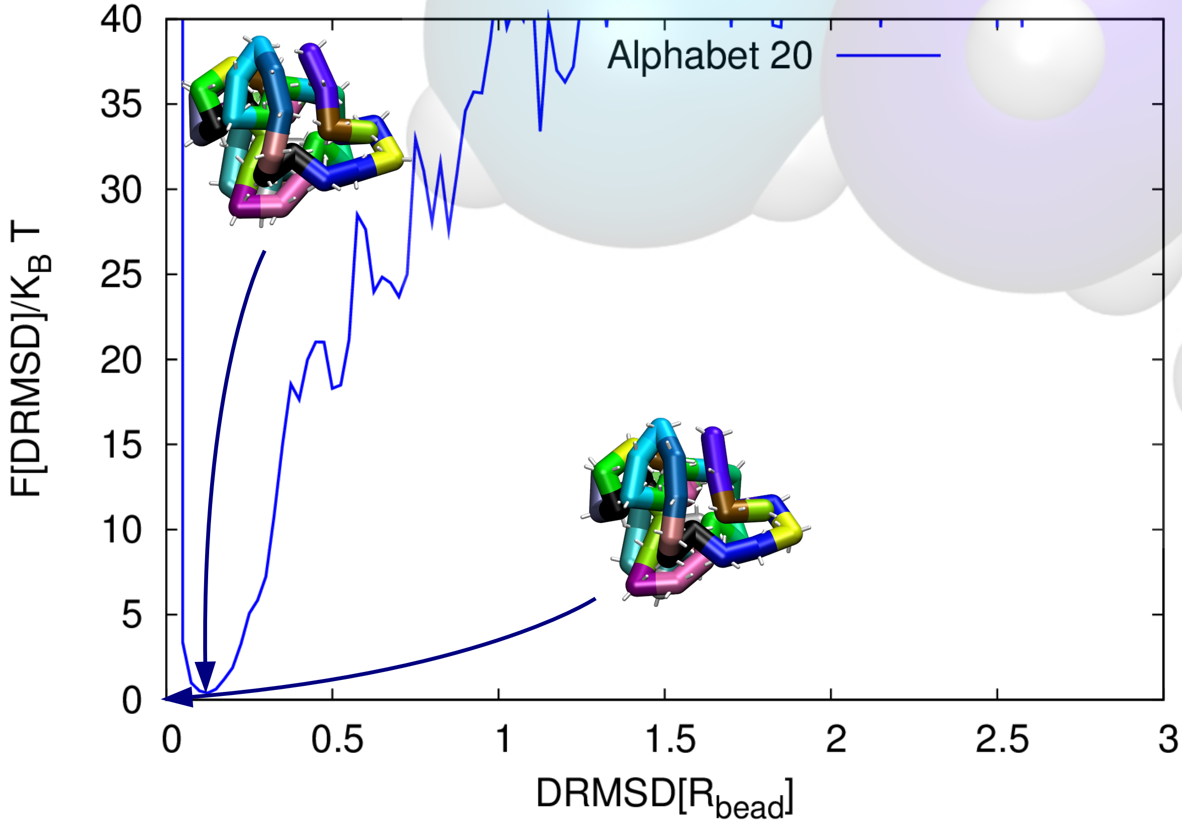
Free energy landscape vs Distance Root Mean Square Displacement (DRMSD) for **three free patches** with **alphabet size of 3**.

How does the folding depend on the alphabet size?



Free energy landscape vs Distance Root Mean Square Displacement (DRMSD) for **three free patches** with **alphabet size of 10**.

How does the folding depend on the alphabet size?



Free energy landscape vs Distance Root Mean Square Displacement (DRMSD) for **three free patches** with **alphabet size of 20**.

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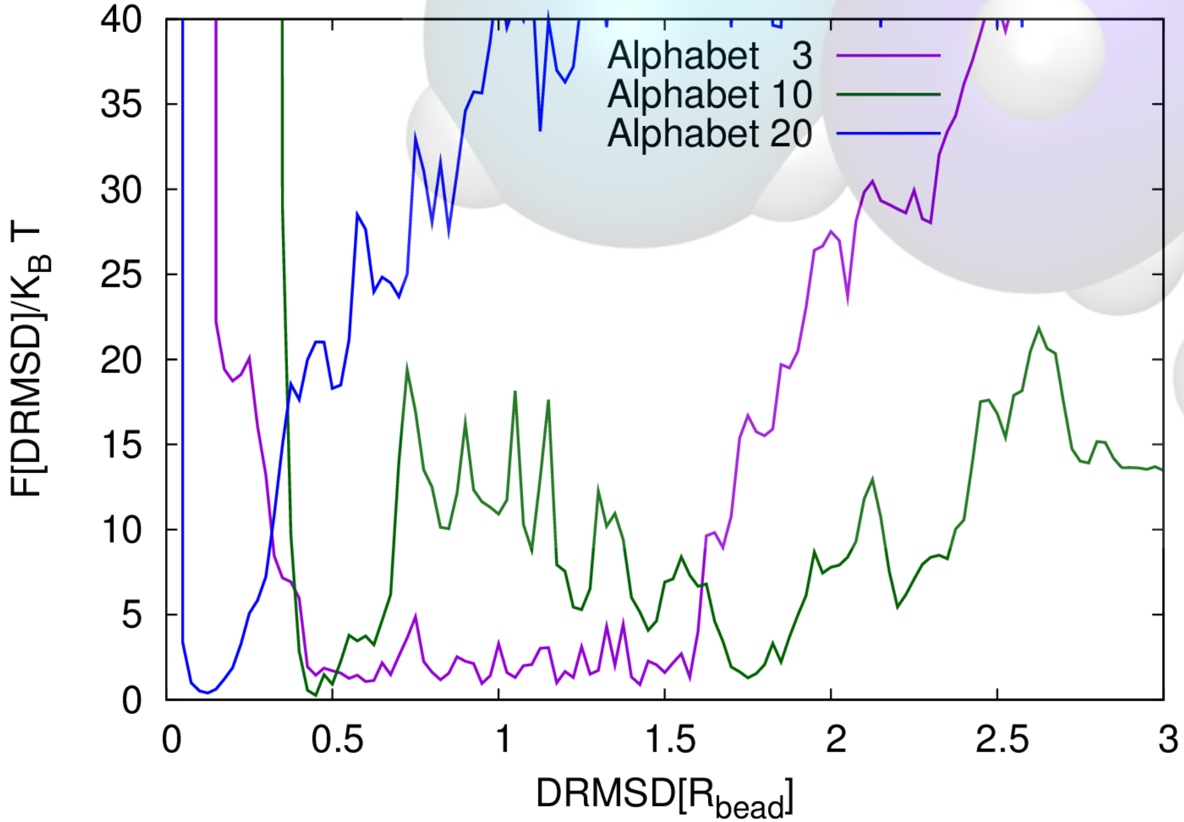
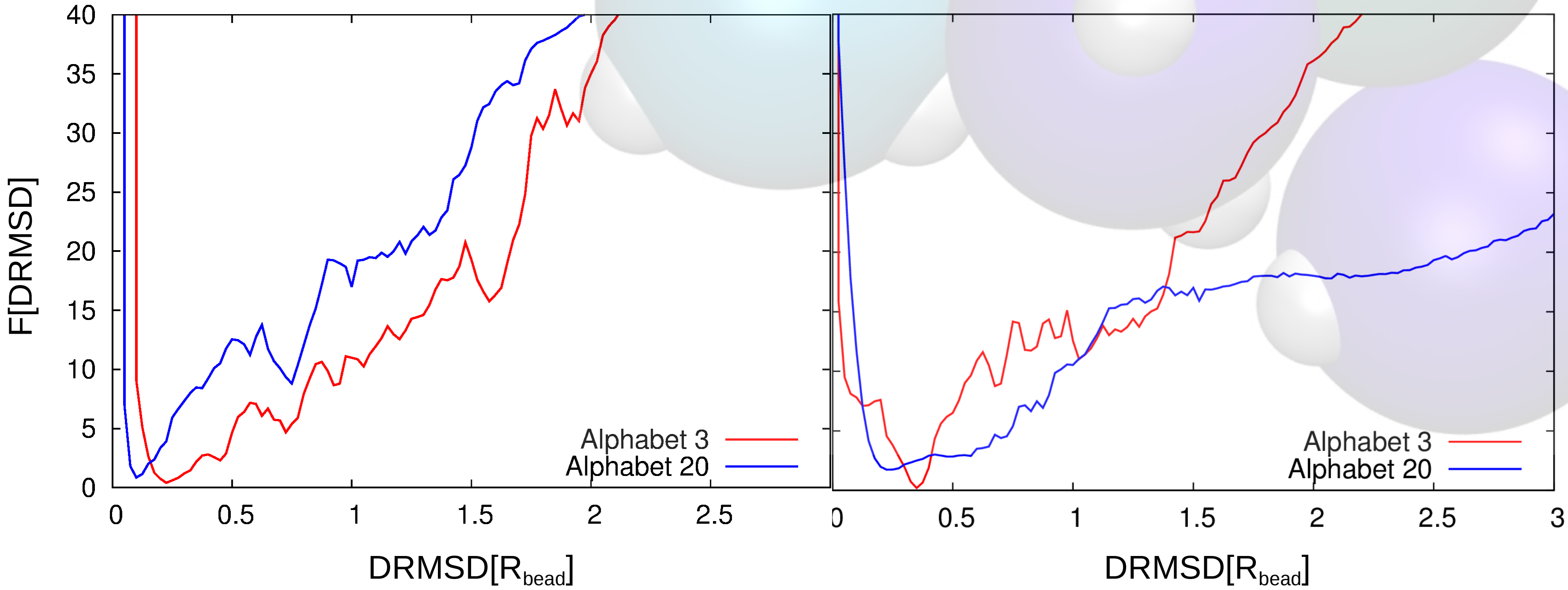
How does the folding depend on the alphabet size?



Free energy landscape vs DRMSD for
three free patches with **different alphabet sizes**.

How does the folding depend on the alphabet size?

1 patch constrained to the backbone 2 patches constrained to the backbone



Free energy landscape vs DRMSD for **one** and **two patches constrained to the backbone** with **different alphabet sizes**. All systems fold into the target structures.

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Conclusions

- Polymers with free patches fold only with large enough alphabets
- Polymers with patches constrained to the backbone fold also with small alphabets

The system is designable if:

The **alphabet** is increased **OR**

The **valence** reduces the space of compact structures (directional interactions: patches)

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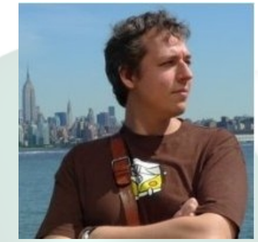
Acknowledgements

- Prof. Christoph Dellago and Dr. Ivan Coluzza



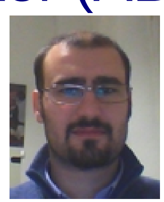
- Theory and simulations of designable modular bionic proteins
  - Dr. Valentino Bianco

FWF Der Wissenschaftsfonds.

- Star polymers with a temperature-dependent valence: empty liquids from soft building blocks
  - Dr. Lorenzo Rovigatti

FWF Der Wissenschaftsfonds.

- Automated Bio Marker (ABM) – In silico automated tumor targeting
  - Dr. Luca Tubiana



interdisciplinarycancerresearch INDICAR

- Computational protein design of highly selective tumour targeting drugs with the Vienna Protein Simulator
  - Msc. Francesca Nerattini

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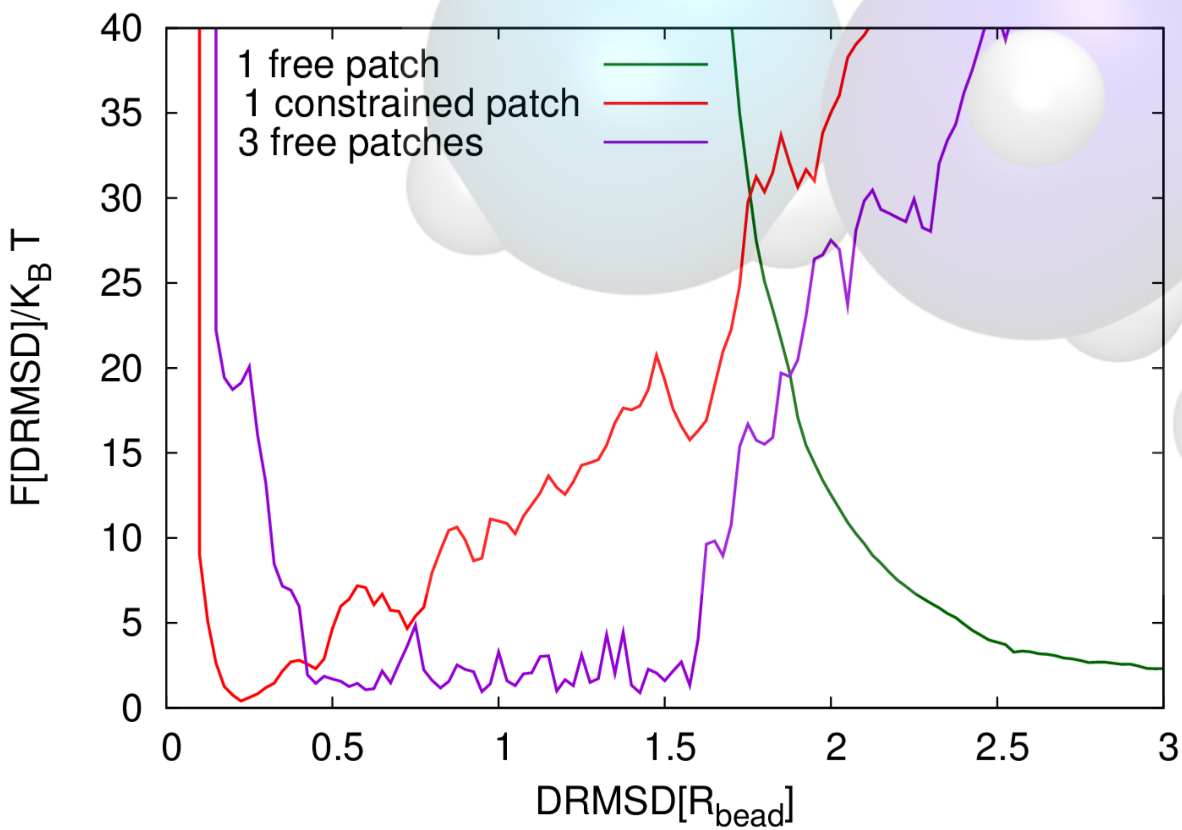
How does the folding depend on the number and the structure of the patches?



Free energy landscape vs DRMSD for three systems with **different valence**. The alphabet size is fixed to 3. Only the structure with one constrained patch folds into the target structure.