DESIGN OF PATCHY POLYMERS
INTERPLAY BETWEEN GEOMETRICAL CONSTRAINS
AND ALPHABET SIZE

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What allows different heteropolymers to fold?
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- Specific sequences fold into stable structures
- Made by 20 different types of amminoacids

Protein
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

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Protein

Protein model on lattice

Specific sequence

Geometrical constrains
Patchy Polymers as bionic proteins

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

Isotropic interaction

Directional interaction

$$\left( \cos(\theta_1) \cos(\theta_2) \right)^2$$
Patchy Polymers as bionic proteins

- Production of novel materials with specific self-assembly properties
Design and Folding of Patchy Polymers
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![Diagram showing the relationship between number of isotropic contacts and number of patches contacts, with an arrow indicating a change in free energy.](image)
Design and Folding of Patchy Polymers

SEEK

DESIGN

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

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?

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

The 3 patches are free to rotate with respect to the backbone.
How does the folding depend on the number and the structure of the patches?

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?

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

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?

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.
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?

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.
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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  Computational protein design of highly selective tumour targeting drugs with the Vienna Protein Simulator

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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.