

Characterization and Structural Analysis of B-cell Epitopes for Vaccine and Therapeutic Antibody Design

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The idea of using peptides as cost-effective vaccines, seems a striking approach for the prevention and treatment of many infectious diseases and malignant disorders [1-2]. Such peptides can be designed synthetically [3] to elicit a response in immune system.

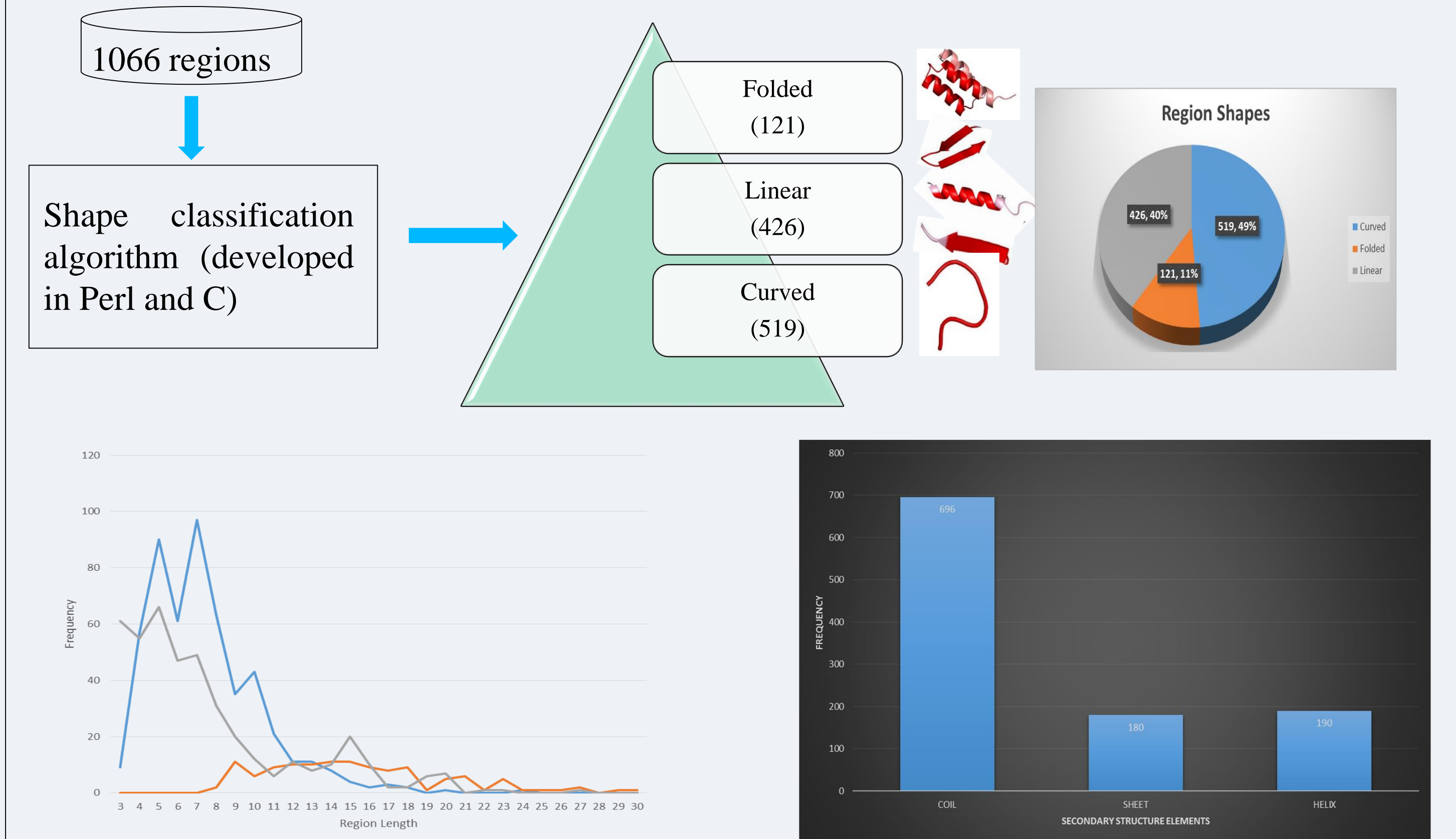
Approximately 83% of B-cell epitopes are conformational in nature with discontinuous regions of the sequence coming together in the 3D fold of the protein and it is therefore important to study how well synthetic peptides are able to mimic these conformations.

Aims: Characterization of B-cell epitopes to inform improved vaccines and antibody design and allow development of peptide vaccine.

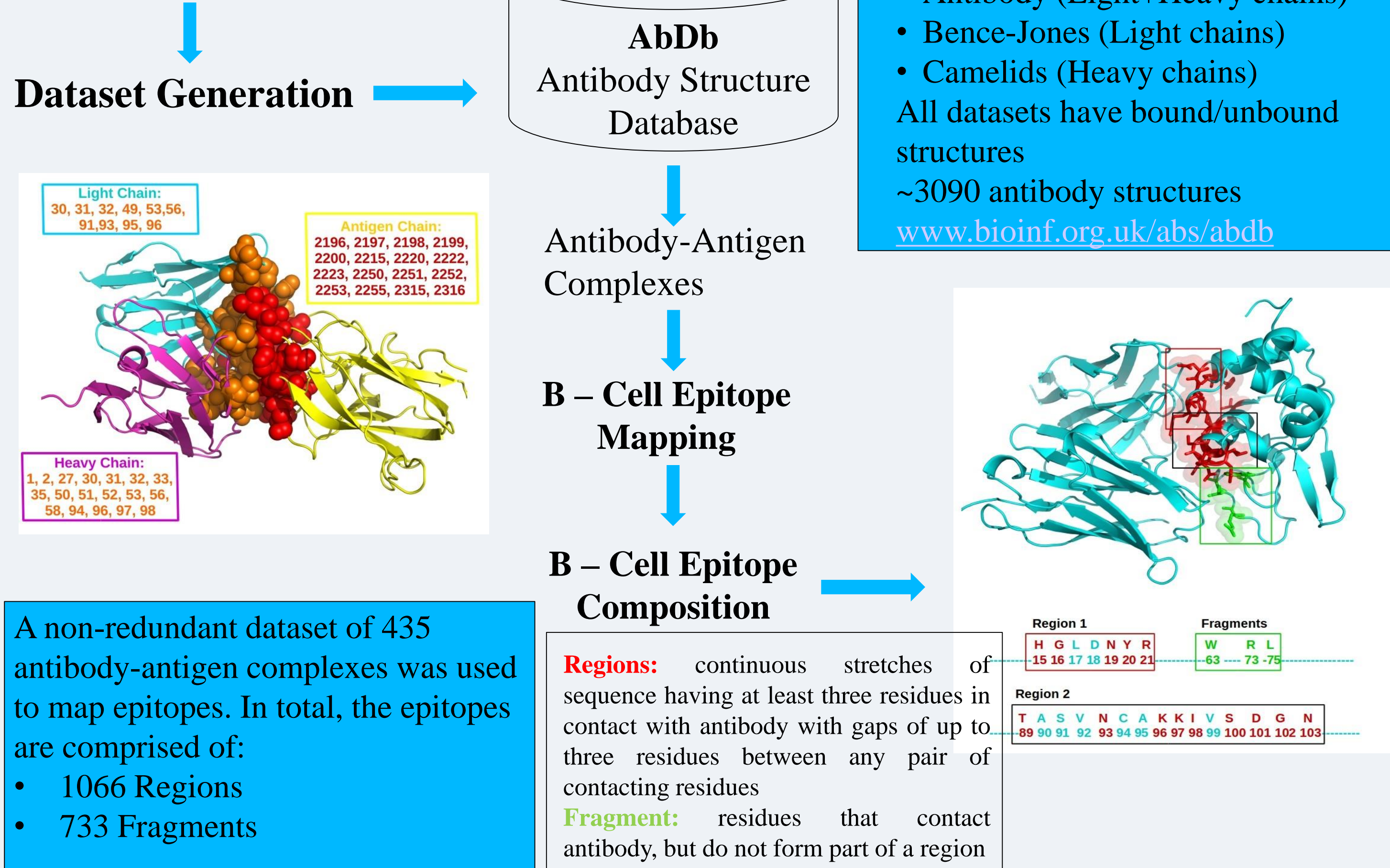
- Advantages:**
- Specificity of Immune Response
 - Exclusion of undesirable Immune response
 - Improving Immunity
 - Cost Effective
 - Ease of Storage/Transport

Epitope Regions' Shape Analysis

Shapes of epitopes were analysed as folded, linear and curved because epitopes are more likely to be represented by peptides.



Design of automated pipeline

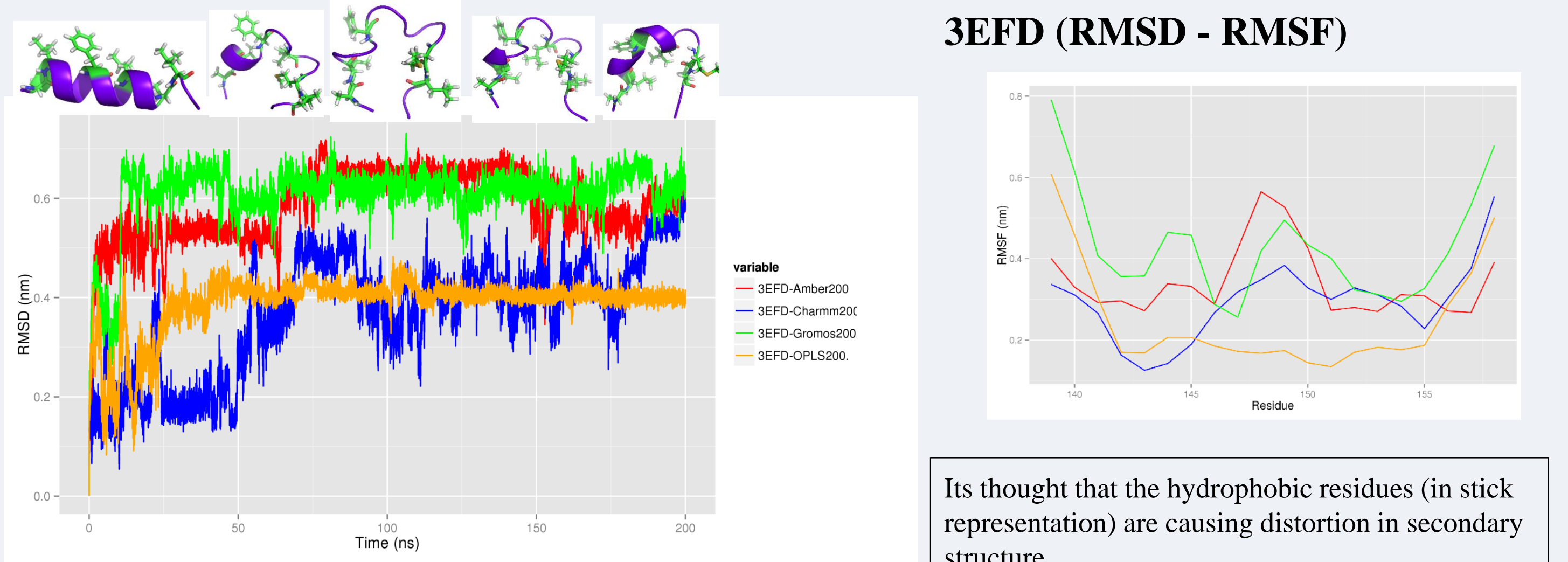


Molecular Dynamics Simulations of Regions

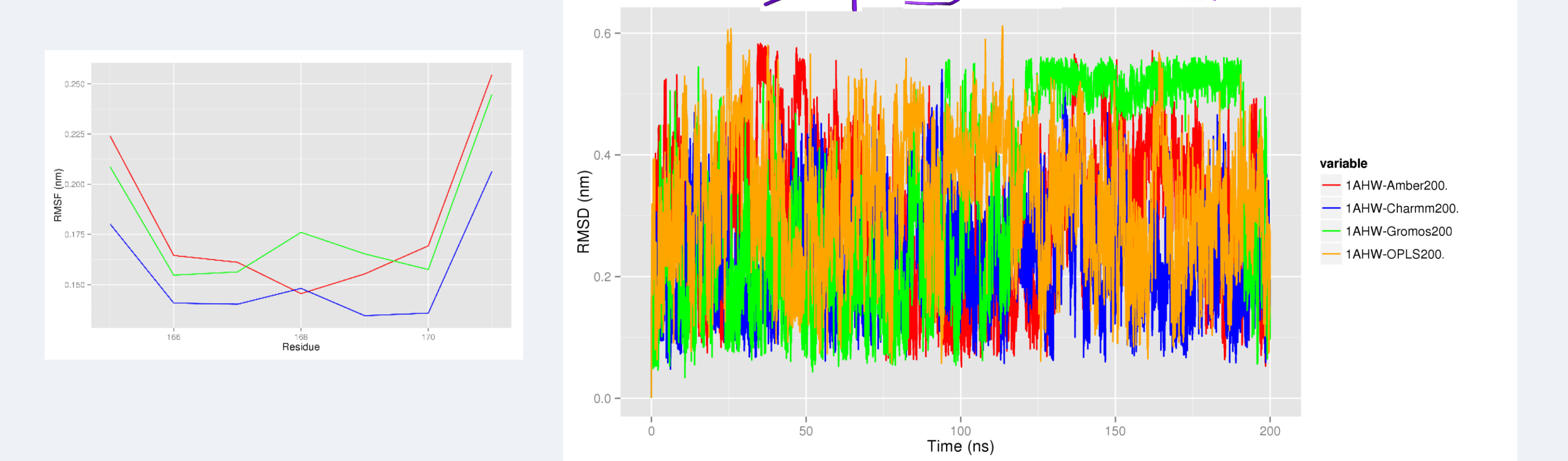
Molecular dynamics simulations were performed to determine that whether isolated peptides adopt the same conformation as in the whole (native) protein.

PDB	Structure	Sequence	Length	Hydrophobicity Score
3EFD	Alpha Helix	RALHERFDRLERMLDD	16	-34.12
1AHW	Beta Strand	KKTAKTN	7	-56.07
3BAE	Loop	AEFRHDS	7	-30.70

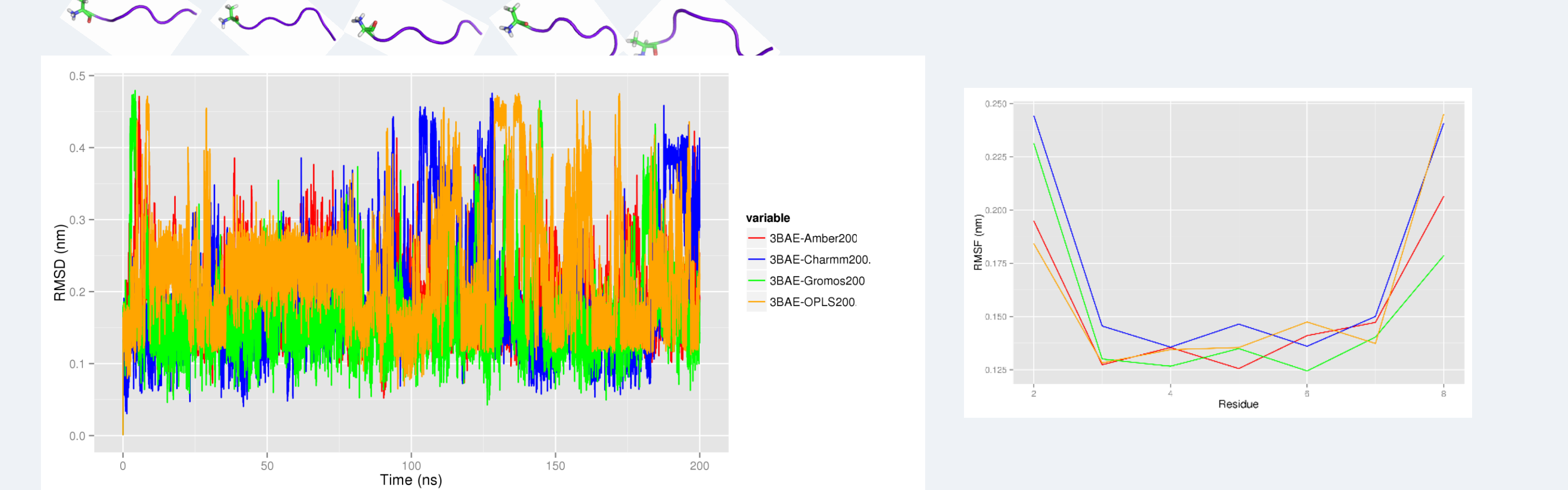
Contact Residues
Hydrophobic residues
Both



1AHW (RMSD - RMSF)



3BAE (RMSD - RMSF)



Future Directions

- Further molecular dynamics simulations of linear and folded regions will be performed to access their conformational stability
- For folded peptides, the effect of stapling the peptides on the dynamics will be explored.
- The mutations will be explored to stabilize the conformations.
- Linkers will be designed for epitopes containing 2 or 3 regions followed by their MD simulations

Epitope Composition Analysis



- Berzofsky, JA. Designing peptide vaccines to broaden recognition and enhance potency. Ann. NY Acad. Sci. 1995. 754:161-168.
- Buteau, C, Markovic, SN, Celis, E. Challenges in the development of effective peptide vaccines for cancer. Mayo Clin. Proc. 2002. 77:339-349.
- Rothbard, J. Synthetic peptides as vaccines. Nature. 1987. 330:106-107.

