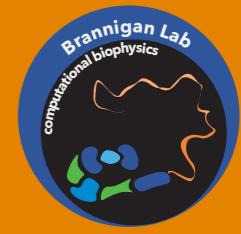


Visualizing Structure with Blobulation: A sequence-based tool for analysis of MD simulations

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Abstract

Blobulation, a sequence-based tool designed to cluster residues in proteins by their hydrophobicity. The blobulator tool finds stretches of hydrophobicity and determine if the length meet our threshold to become a hydrophobic cluster or h-blob. Certain forms of these clusters are found in disease associated Single Nucleotide Polymorphisms (dSNPs)[2]. There's been a prevailing need for blobulation to have a 3D representation for both clarity and analysis. Having an interactive blobulation tool that allows the user to see hydrophobic clusters in a 3D space, offers added insight into protein structure. Here, we show off the functions of this graphical representation, it's utility, and it's user experience.

Visualization Options

- Visual Molecular Dynamics (VMD) offers graphical representation options
- These give different interpretations of the same protein
- VMD Representations don't often show hydrophobic regions

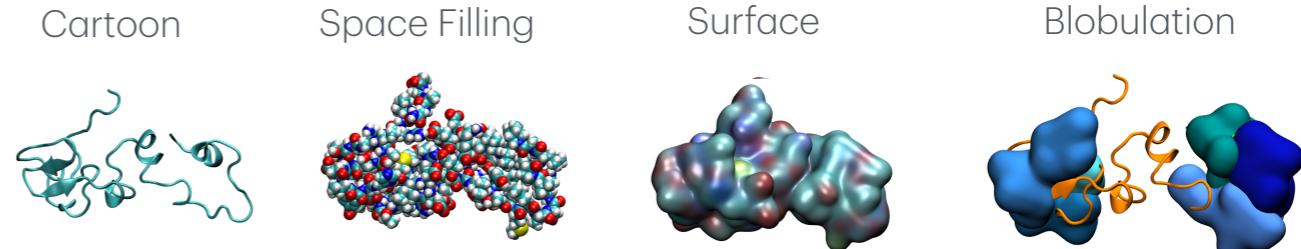


Figure 1. Brain Derived Neurotrophic Factor pro domain an intrinsically disordered protein. Each image uses a different graphical representation (New Cartoon, VDW, Quicksurf, and Blobulation)

Background

- Blobulator is an algorithm that creates subsequence clusters determined by hydrophobicity [1].
- Currently, there's a Blobulator web app that shows hydrophobicity in a sequence but no 3D representation..
- Visual Molecular Dynamics (VMD) is the most widely used software for visualizing molecular dynamics trajectories.

Blobulation Algorithm

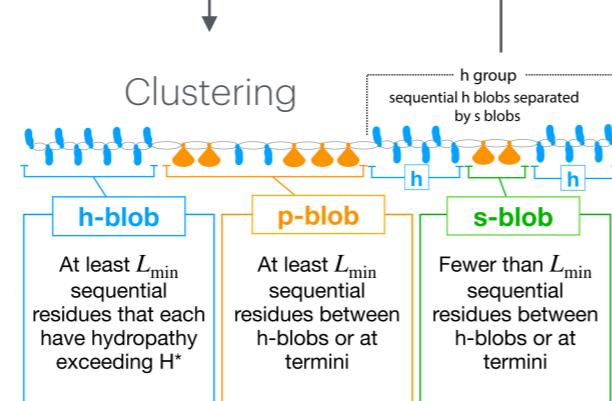
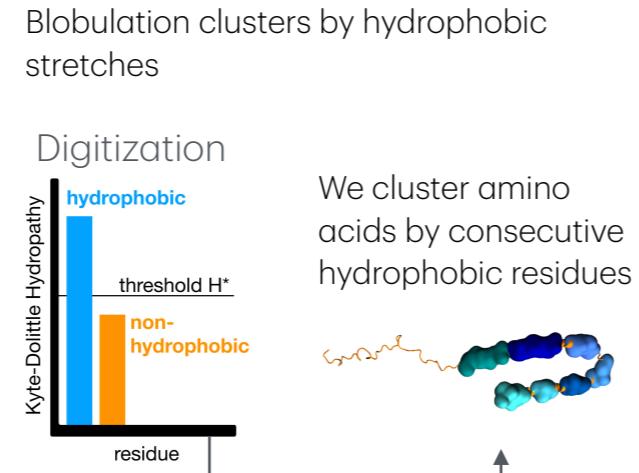


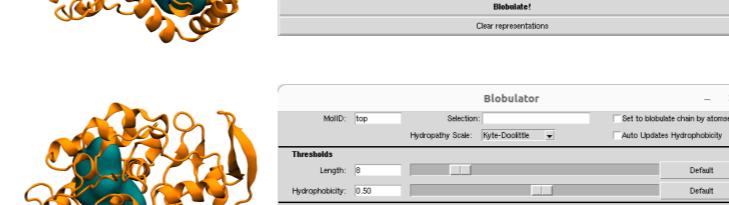
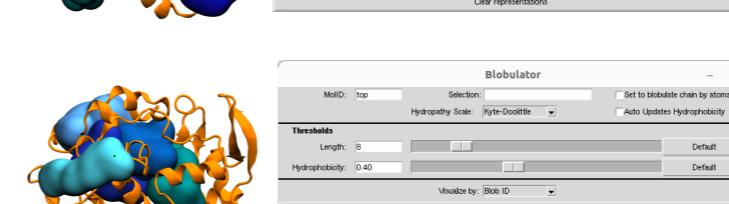
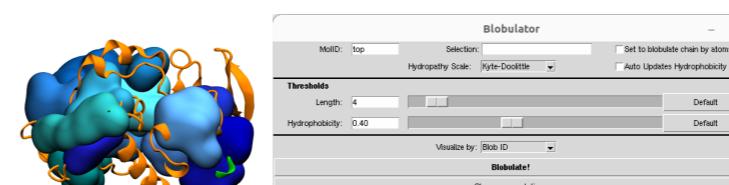
Figure 2: Blobulation, a sequence based approach for determine hydrophobic regions. Our algorithm determines a residues hydrophobicity (left). And determines if any stretch of hydrophobicity reaches our length threshold. 'H', 'P', and "S" refer to "hydrophobic" "polar" " and short blobs respectively (below). From there we can create a blobulated sequence of Alpha Synuclein (1xq8) (right). [2]

Developer Goals

- Recreate the Blobulator algorithm, from the ground up, using the TCL backend of VMD
- Allow use of different length thresholds, hydrophobicity thresholds, and hydrophobicity scales
- Store blob information in a way that can be accessed by the visual display
- Create a GUI frontend for better user experience.

Finding strong hydrophobic clusters

- VMD Blobulator GUI allows changes on the fly!
- Adjusting parameters makes the criteria for h-blobs more strict or more lax
- Increased strictness allows a user to detect the most hydrophobic blobs, usually at the protein core



Hydrophobicity Scales

Different hydropathy scales offer a different measurements for hydrophobicity



Kyte-Doolittle



Eisenberg-Weiss



Moon-Fleming

Figure 4. Alpha synuclein (1xq8) blobulated with different hydropathy scales

The Road Ahead

- Fix known issues, reported on Github page
- Make blobulation an official draw style for VMD
- Optimize code to help alleviate long load times for large proteins

References

1. Lohia R, Salari R, Brannigan G. PLoS Comput Biol. 2019
2. Lohia, R., Hansen, M. E., & Brannigan, G. PNAS (2022).