HullRad Description

August, 2024

HullRad is an algorithm for calculating hydrodynamic properties of a macromolecule from a structure file (PDB or mmCIF). Many of these properties are directly relevant to interpretation of AUC results.

The list of properties calculated by HullRad is extensive. It provides:

Mass, M
Partial specific volume, $\bar{v}$
Molecular volume, R_0
Radius of Gyration, R_G
Maximum dimension, D_{MAX}
Axial ratio, a/b
Frictional ratio, f/f_0
Translational diffusion coefficient, D_T
Stokes radius, R_S (also called translational hydrodynamic radius, R_T)
Sedimentation coefficient, $s_{20,W}$
Intrinsic viscosity, $[\eta]$
Total hydration, g/g
Hydrated Specific Volume, mL/g
Sedimentation velocity non-ideality constant, k_S
Diffusion non-ideality constant, k_D
Second virial coefficient from volume exclusion, B_{EX}
Asphericity, δ
Rotational diffusion coefficient, D_R
Rotational hydrodynamic radius, R_R
Rotational correlation time, τ_C

HullRad works with proteins, glycoproteins, DNA, RNA, and several detergents (for membrane proteins in micelles).

The fundamental calculation of HullRad is the hydrodynamic volume of a macromolecule using a convex hull construct. This makes HullRad very fast. It also enables calculation of the amount of water associated with the macromolecule in terms of total hydrodynamic volume.

Details for the calculation of the above properties may be found in three publications describing the validation and use of HullRad:

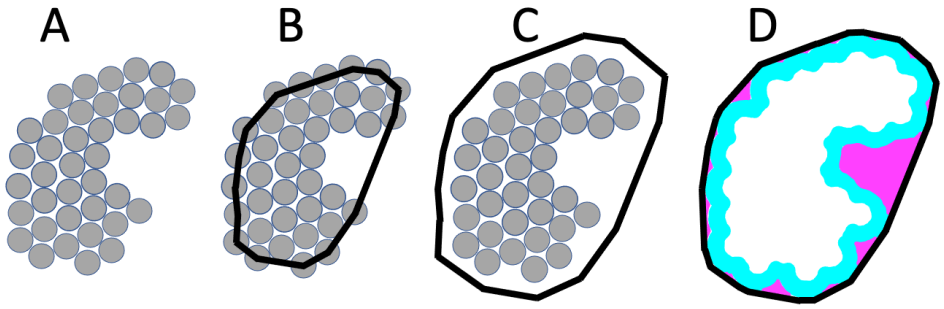
1. Fleming PJ, Fleming KG. HullRad: Fast Calculations of Folded and Disordered Protein and Nucleic Acid Hydrodynamic Properties. *Biophysical Journal.* 2018 114(4):856–69.
   (The original description and validation of HullRad.)
   DOI: 10.1016/j.bpj.2018.01.002

2. Fleming PJ, Correia JJ, Fleming KG. Revisiting macromolecular hydration with HullRadSAS. *European Biophysics Journal*. 2023 52(4–5):215–24.
   (A description of the hydrodynamic water associated with a macromolecule.)
   DOI: 10.1007/s00249-022-01627-8

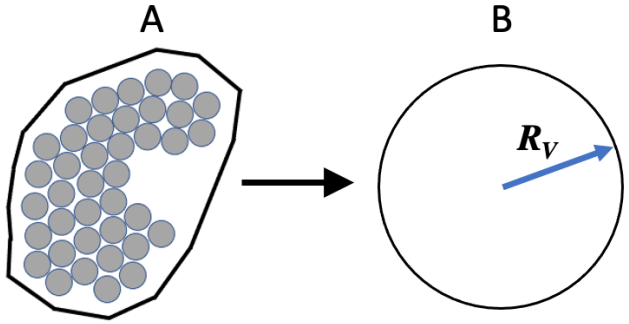
3. Fleming, PJ, Corriea, JJ and Fleming, KG. The Molecular Basis for Hydrodynamic Properties of PEGylated Human Serum Albumin. *Biophysical Journal*, Online June 21, 2024. (Description of the implementation of solution non-ideality constant calculations in HullRad.)
DOI: 10.1016/j.bpj.2024.05.019

HullRad Algorithm*

The method uses a convex hull to estimate the hydrodynamic volume of the macromolecule. The figure below is a two-dimensional representation of three-dimensional objects and illustrates the method. (A) Macromolecular atoms represented as grey circles. (B) Initial convex hull (thick black line) constructed through atom centers. (C) Final convex hull expanded to encapsulate first shell hydration. (D) First shell (cyan) and entrained (magenta) water are encapsulated by the final convex hull (black). Both types of water are necessary components of the hydrodynamic volume.



From the volume of the final convex hull, the macromolecular hydrodynamic equivalent volume radius R_V is determined by constructing an equivalent volume sphere as shown in the figure below. A molecular model with single pseudo-atom side chains is used to calculate the convex hull. This conversion to a single pseudo-atom side chain averages rotamer conformations.



The radius of a sphere (B) with equivalent volume of the final convex hull (A, black line) is the hydrodynamic equivalent volume radius R_V of a macromolecule. From the axial ratio of the best fit ellipsoid of revolution to the convex hull a Perrin-like shape factor f_P is determined. The macromolecular Stokes radius is calculated by multiplying the hydrodynamic volume radius by the shape factor, $R_S = f_P * R_V$. The diffusion coefficient at 20°C in water and infinite dilution $D^0_{20,W}$ is calculated using the Stokes-Einstein-Sutherland equation,

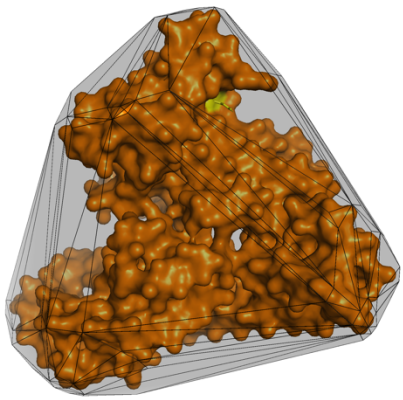
$$D^0_{20,W} = \frac{RT}{N_A 6\pi\eta R_s}$$

the equivalent sedimentation coefficient $s^0_{20,W}$ is calculated using the Svedberg equation,

$$s^0_{20,W} = \frac{M(1-\bar{\nu}\rho)}{N_A 6\pi\eta R_s}$$

Many of the other properties calculated by HullRad derive from the Stokes radius and the expressions are detailed in the references listed above.

The single pseudo-atom side chain model of human serum albumin is shown below as a molecular surface (orange) encapsulated by its corresponding final convex hull (grey planes with black edges).



*Modified from the Supplemental Information accompanying reference 3 above.

HullRadSAS is a second version of HullRad that uses a solvent accessible surface for constructing the convex hull. Note that this alternate algorithm used in HullRadSAS distinguishes between first shell hydration water and entrained hydrodynamic water, the original HullRad only provides the total of the two. HullRadSAS also provides a hydrated R_G suitable for comparison to experimental SAXS results. The other properties listed above are the same as the original HullRad. HullRadSAS is slower than HullRad so, if you do not need to know the separate amounts of first shell and entrained water, or are comparing R_G to SANS results and not SAXS, use the original HullRad.

Citing HullRad

If you publish data calculated by HullRad that relates to sedimentation coefficients, Stokes radii, or diffusion coefficients please cite reference 1 above; for data relating to hydration and hydrodynamic volume please cite reference 2 above; for non-ideality results, reference 3.

HullRad Code

You can download the HullRad or HullRadSAS python scripts for use on your own computer. They are available under the Download Code tab or under the HullRadSAS tab on the website (hullrad.jhu.edu). Python3 with numpy, scipy, and biopython (for HullRadSAS) are required to run the scripts.