

US-SOMO (SOLution MOdeler): versatile and reliable hydrodynamic and SAS modeling of biomacromolecules within the UltraScan AUC data analysis software

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Hydrodynamics.

Stokes-Einstein's law

The translational frictional coefficient of f a sphere of radius r in a solvent of viscosity η is:

$$f = 6\pi\eta r$$

For a body of unknown shape having a translational frictional coefficient f , we can define the Stokes radius R_s as that of a sphere having the same f

$$R_s = r = f/6\pi\eta$$

Translational diffusion coefficient D_t :

$$D_t = k_b T / f$$

where k_b = Boltzmann's constant

T = solution temperature ($^{\circ}\text{K}$)

Sedimentation coefficient s :

$$s = (M/N_0)(1 - v_2\rho)/f$$

where M = mass

N_0 = Avogadro's number

v_2 = partial specific volume

ρ = solvent density

Early applications of hydrodynamics: representing proteins as simple geometrical objects (spheres, ellipsoids of revolution)

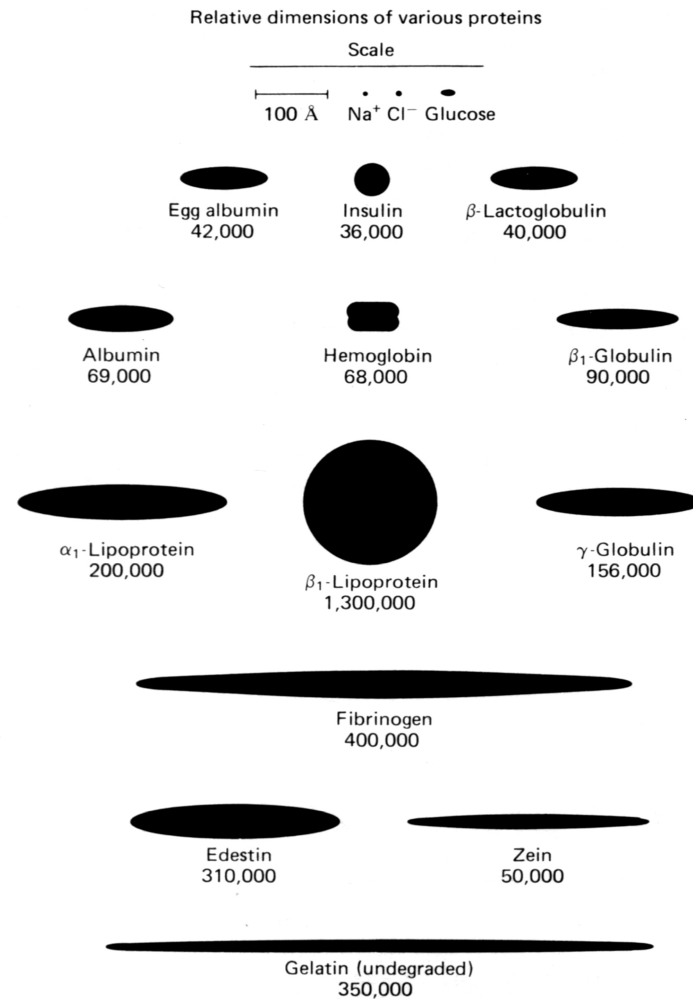
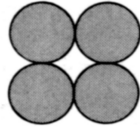
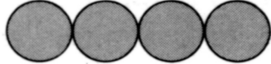
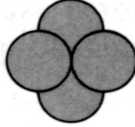
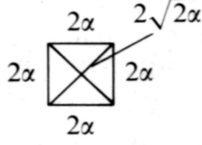
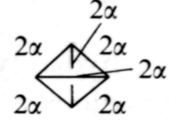
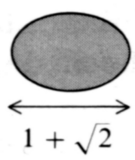
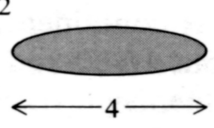



FIGURE 7-25. Dimensions of the ellipsoid of revolution that best account for the hydrodynamic properties (viscosity and frictional coefficient) of various protein molecules. [After W. J. Moore, *Physical Chemistry*, Prentice-Hall, Englewood Cliffs, N. J., 1972.]

Early applications of hydrodynamics: representing proteins as simple geometrical objects (spheres, ellipsoids of revolution)

Subunit arrangement			
Distances (each counted twice in Eqn. 10-33)		$ 2\alpha + 2\alpha + 2\alpha $ $ 4\alpha $ $ 4\alpha $ $ 6\alpha $	
f/f_{monomer}	1.70	1.92	1.60
f relative to tetrahedron	1.06	1.20	1.00
Ellipsoid model			 (Sphere)
f/f_{sph} from Eqn. 5-12	1.07	1.18	1.00

The ‘hydration’ issue

Cantor and Schimmel - Biophysical Chemistry Part II, 1980

12-1 VISCOMETRY

655

Table 12-2

Hydrations of biopolymers computed by using shapes known from x-ray diffraction or electron microscopy

Sample	Known axial ratio [§]	Hydration (δ_1 in g/g) based on		
		Viscosity	Diffusion	Sedimentation
Bushy stunt virus	1.0	0.65	0.71	0.71
Carboxypeptidase	1.25	—	0.30	0.69
Cytochrome <i>c</i>	1.48	—	0.18	0.24
Hemoglobin	1.3	0.62	0.52	0.75
Lysozyme	1.5	0.34	0.52	0.52
Myoglobin	1.76	0.44	0.50	0.42
Tobacco mosaic virus	18	0.32	0.1–0.7	0.26

[§] Axial ratios are for prolate ellipsoids, except for cytochrome *c*, which is oblate.

SOURCE: After I. D. Kuntz, Jr., and W. Kauzmann, in *Advances in Protein Chemistry*, vol. 28, ed. C. B. Anfinsen, J. T. Edsall, and F. M. Richards (New York: Academic Press, 1974), p. 239.

Advances in Protein Chemistry 28:239-345, 1974

HYDRATION OF PROTEINS AND POLYPEPTIDES

By I. D. KUNTZ, JR. and W. KAUZMANN

Department of Pharmaceutical Chemistry, University of California, San Francisco, California,
and Department of Chemistry, Princeton University, Princeton, New Jersey

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Hydration from NMR freezing experiments

I. D. KUNTZ, JR. AND W. KAUZMANN

HYDRATION OF PROTEINS AND POLYPEPTIDES

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TABLE XXII
Proposed Amino Acid Hydrations Based on Nuclear
Magnetic Resonance Studies of Polypeptides^a

Amino acid residues ^b	Hydration ^c
Ionic	
Asp ⁻	6
Glu ⁻	7
Tyr ⁻	7
Arg ⁺	3
His ⁺	4 ^d
Lys ⁺	4
Polar	
Asn	2
Gln	2 ^e
Pro	3
Ser, Thr	2 ^e
Trp	2 ^e
Asp	2
Glu	2
Tyr	(3)
Arg	3
Lys	4
Nonpolar	
Ala	1
Gly	1
Phe	(0)
Val	1
Ile, Leu, Met	1 ^e

^a After Kuntz (1971a).

^b Standard three-letter code.

^c Moles of water per mole of amino acid.

^d As Lys⁺.

^e Assumed values based on one water molecule per amide plus one water molecule per side-chain polar group.

TABLE XXIII
Prediction of Protein Hydration from Composition and Polypeptide Results^a

Protein, native	Hydration (g H ₂ O/g protein)	
	Calculated ^b	Observed ^c
Lysozyme	0.36	0.34
Myoglobin	0.45	0.42
Chymotrypsinogen	0.39	0.34
Chymotrypsin	0.36	0.33
Ovalbumin	0.37	0.33
Bovine serum albumin (BSA)	0.45	0.40
Hemoglobin (denatured)	0.42	0.42
BSA + urea	0.45	0.44
BSA, pH 3	0.32 ^d	0.30

^a After Kuntz (1971a); see Table XXII.

^b Calculation assumes that *all* residues are fully hydrated. This is perhaps reasonable for the denatured proteins but leads to a small positive error unless allowance is made for "buried" groups. This correction was done for lysozyme, yielding a calculated value of 0.335.

^c NMR freezing experiments.

^d Calculation assumes that all carboxyl groups are uncharged at pH 3.

Reconciling hydration dynamics with hydrodynamics

PNAS 100:12135-12140, 2003

Biomolecular hydration: From water dynamics to hydrodynamics

Bertil Halle* and Monika Davidovic

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1-The static picture of biomolecular hydration is fundamentally inconsistent with magnetic relaxation dispersion experiments and molecular dynamics simulations, which both reveal a highly dynamic interface where rotation and exchange of nearly all water molecules are several orders of magnitude faster than biomolecular diffusion.

2-Waters near the biomolecular surface have a different density, and alter the local viscosity. It turns out that considering a number of “tightly bound”, static water molecules compensate well for this local viscosity effect, otherwise very hard to be directly taken into account.

Bead modeling methods: from an idea of V. Bloomfield, further developed by D.C. Teller, to HYDROPRO (J. García de la Torre)

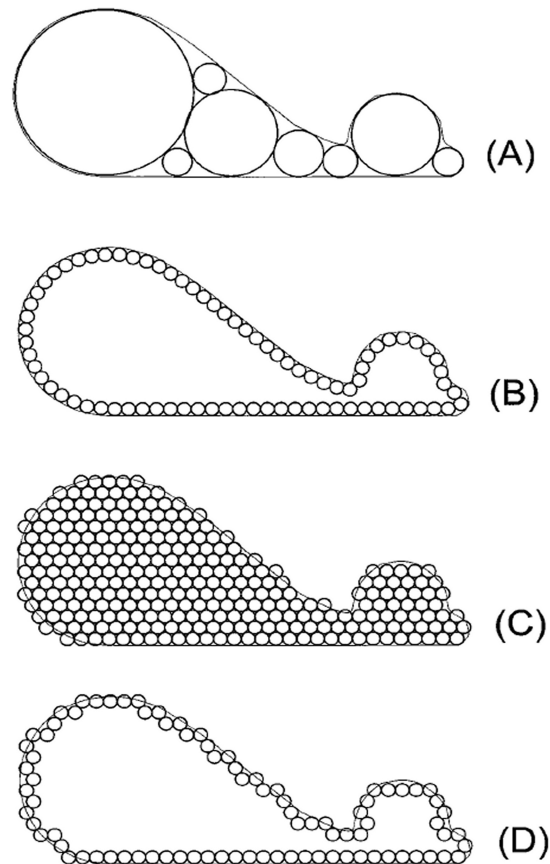


FIGURE 1 Two-dimensional analogies of the various model types. (A) A bead model (in strict sense). (B) Shell model. (C) Filling model. (D) Rough-shell model.

Carrasco & García de la Torre
Bioph. J. 75, 3044-3057, 1999

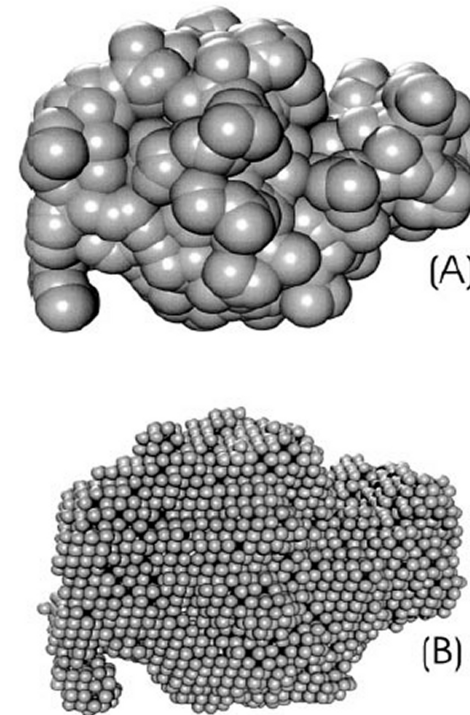


FIGURE 2 (A) A bead-per-atom (BPA) model of lysozyme, which we take as the primary hydrodynamic particle (PHP) that represents this protein. The atomic element radius (AER) is $a = 3 \text{ \AA}$. (B) A shell model (SHE), derived from the PHP, used for hydrodynamic calculations. The radius of the small beads in this case is $\sigma = 0.8 \text{ \AA}$.

García de la Torre, Huertas & Carrasco
Bioph. J. 78, 719-730, 2000

Low Reynolds number hydrodynamics

$$\begin{pmatrix} \mathbf{F} \\ \mathbf{T}_O \end{pmatrix} = \begin{pmatrix} \underline{\Xi}_t & \underline{\Xi}_{O,c}^T \\ \underline{\Xi}_{O,c} & \underline{\Xi}_{O,r} \end{pmatrix} \begin{pmatrix} \mathbf{u}_O \\ \boldsymbol{\omega} \end{pmatrix}$$

$$\mathbf{F}_i (6\pi \eta_0 \sigma_i)^{-1} + \sum_{j=1}^N \mathbf{T}_{ij} \cdot \mathbf{F}_j = (\mathbf{u}_i - \mathbf{v}_i^0)$$

$$\mathbf{T}_{ij} = (8\pi \eta_0 R_{ij})^{-1} \left[\mathbf{I} + \frac{\mathbf{R}_{ij} \mathbf{R}_{ij}}{R_{ij}^2} + \frac{(\sigma_i^2 + \sigma_j^2)}{R_{ij}^2} \left(\frac{1}{3} \mathbf{I} - \frac{\mathbf{R}_{ij} \mathbf{R}_{ij}}{R_{ij}^2} \right) \right]$$

$$\sum_{j=1}^N \mathbf{B}_{ij} \cdot \mathbf{F}_j = (\mathbf{u}_i - \mathbf{v}_i^0) \quad \mathbf{B}_{ij} = \delta_{ij} \frac{\mathbf{I}}{6\pi \eta_0 \sigma_i} + (1 - \delta_{ij}) \mathbf{T}_{ij} \quad \mathbf{C} = \mathcal{B}^{-1}$$

$$\underline{\Xi}_t = \sum_i \sum_j \mathbf{C}_{ij} \quad \underline{\Xi}_{O,c} = \sum_i \sum_j \mathbf{U}_i \cdot \mathbf{C}_{ij} \quad \underline{\Xi}_{O,r} = -\sum_i \sum_j \mathbf{U}_i \cdot \mathbf{C}_{ij} \cdot \mathbf{U}_j + 6\eta_0 \mathbf{V} \mathbf{I}$$

TO COMPUTE THE PARAMETERS THAT CAN BE MEASURED EXPERIMENTALLY, A COMPROMISE MUST BE REACHED BETWEEN A GOOD REPRESENTATION OF THE SURFACE OF THE PROTEIN AND A LOW NUMBER OF FRICTIONAL ELEMENTS (BEADS).

THE LAYER OF “TIGHTLY BOUND” WATER OF HYDRATION MUST ALSO BE TAKEN INTO ACCOUNT

Early programs developed by the Byron/Rocco groups:

BEAMS (BEADs Modeling System) Spotorno et al., *Eur. Biophys. J.* 25, 373-384, 1997.

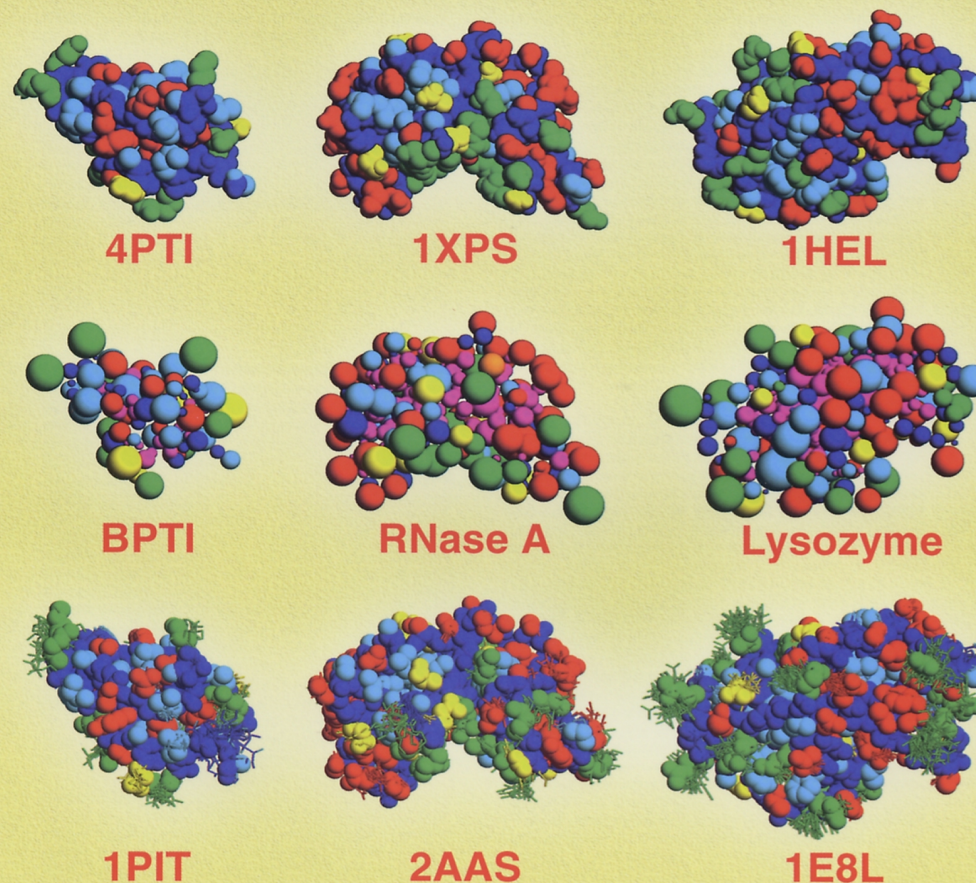
AtoB
Byron, *Biophys J.* 72, 408-415, 1997.

SOMO (SOLution MOdeler)
Rai et al., *Structure* 13, 723-744, 2005;

Structure

Volume 13 Number 5

May 2005



**Side Chain Flexibility
and Protein Hydrodynamics**

Method *SOMO* (SOLution MOdeller): generating medium-resolution bead models from atomic coordinates

Main features:

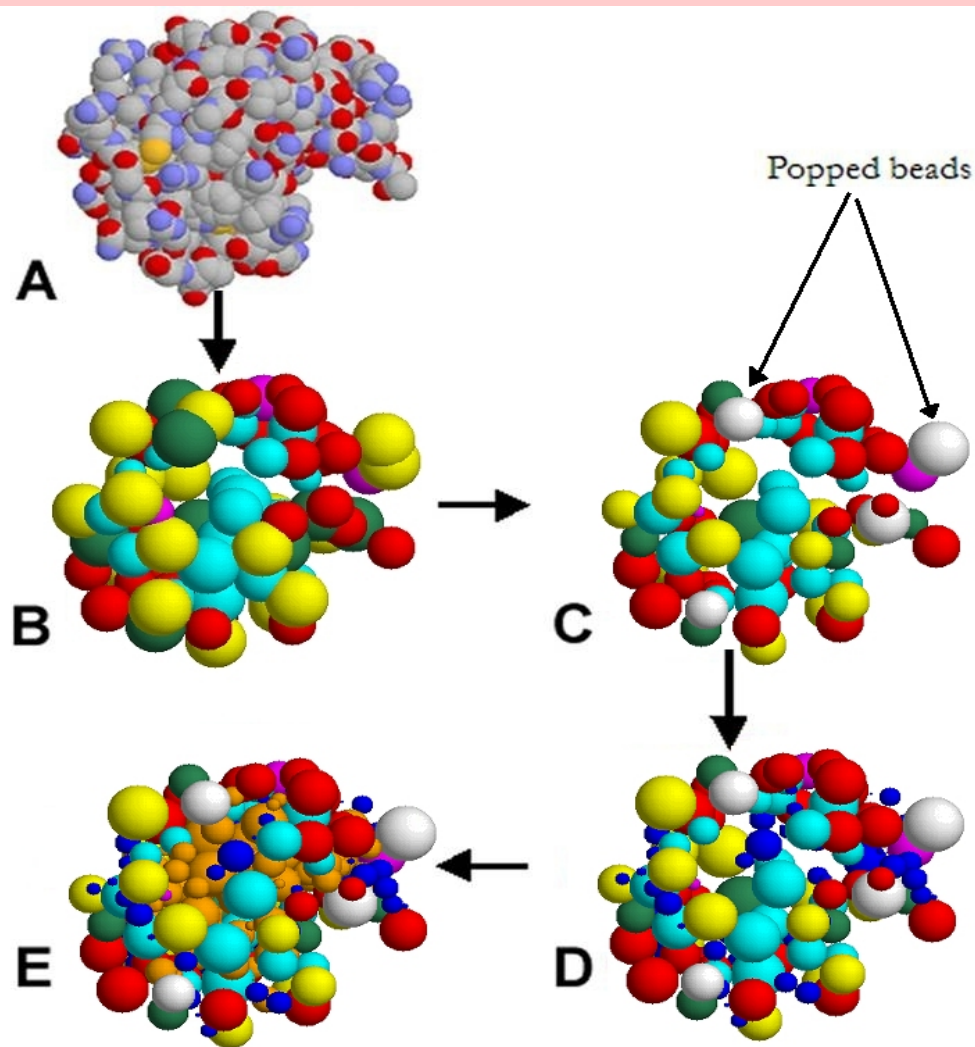
1 bead/side chain & 1 bead/main chain.
Water of hydration, based on residues, is included in each bead.

A→B After ASA screening, exposed **side**-chains beads are placed.

B→C Beads overlapping by more than a preset threshold can be fused together. Overlaps are then removed, reducing the radii and outward translating the centers of exposed beads.

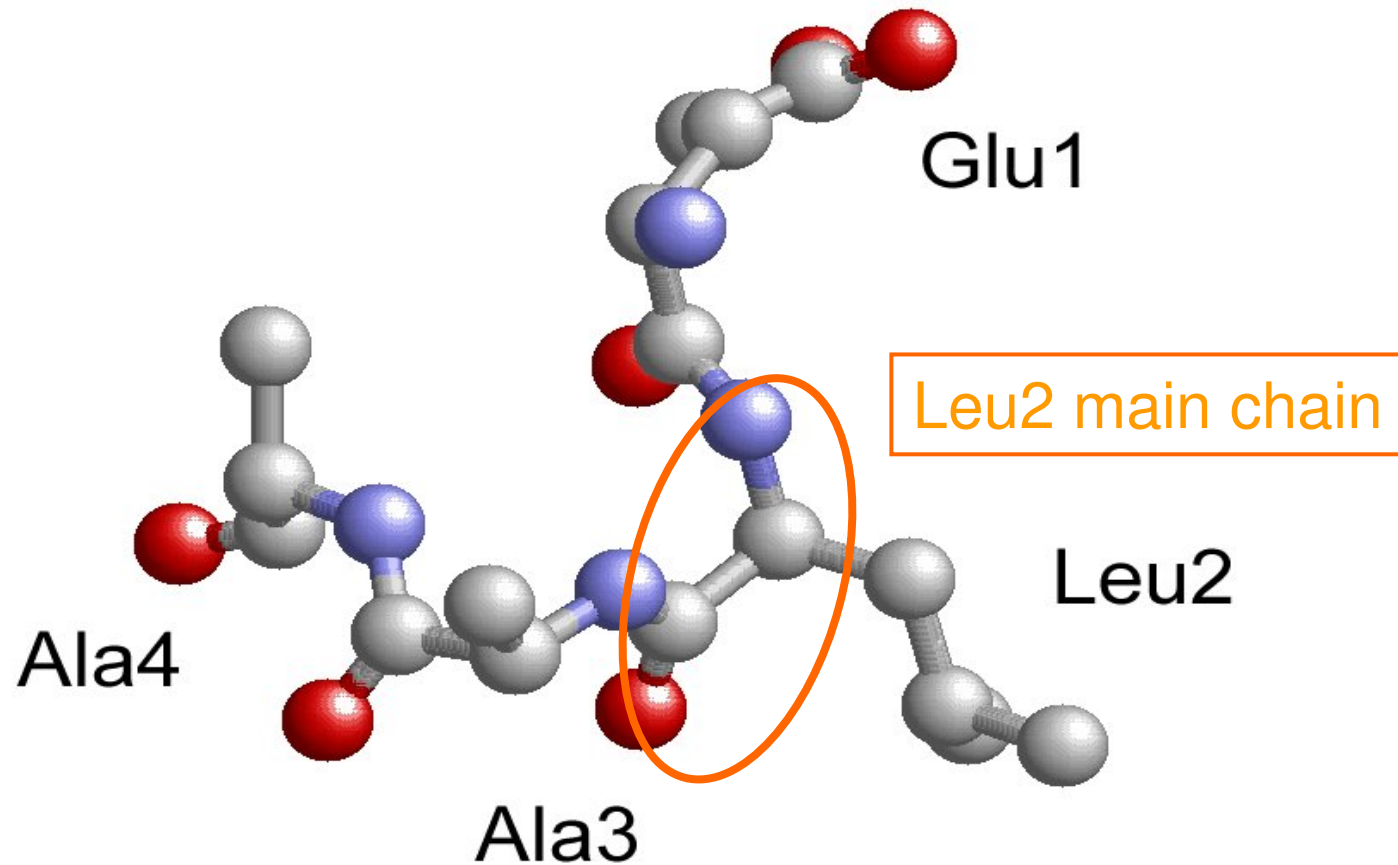
C→D Exposed **peptide bond** beads are placed and overlaps removed.

D→E **Buried beads are placed and overlaps removed.** They should be excluded from the computations of the hydrodynamic parameters.

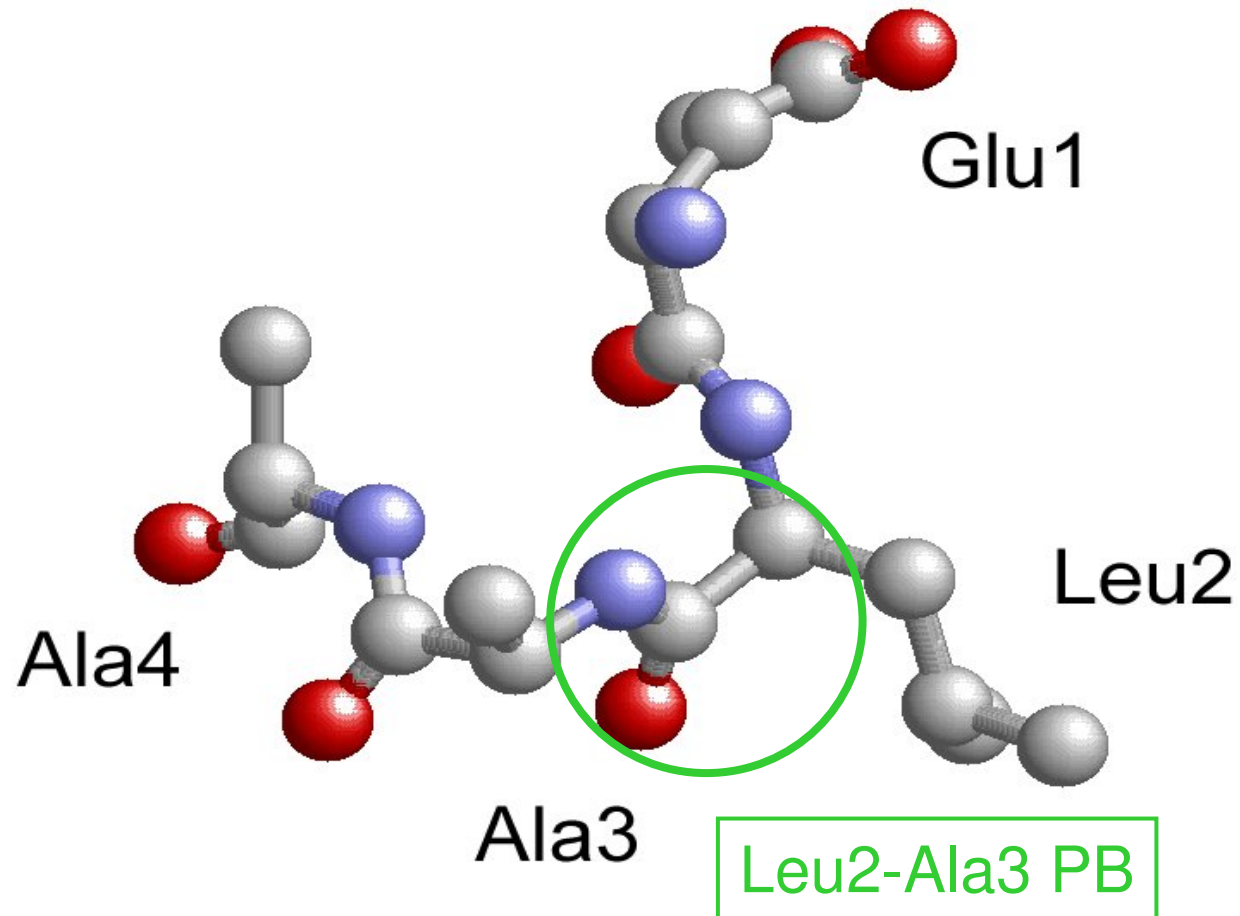


Rai et al., *Structure*, May 2005

The “peptide bond” rule



The “peptide bond” rule



Improved AtoB (Grid) method: generating variable-resolution bead models from atomic coordinates

Main features:

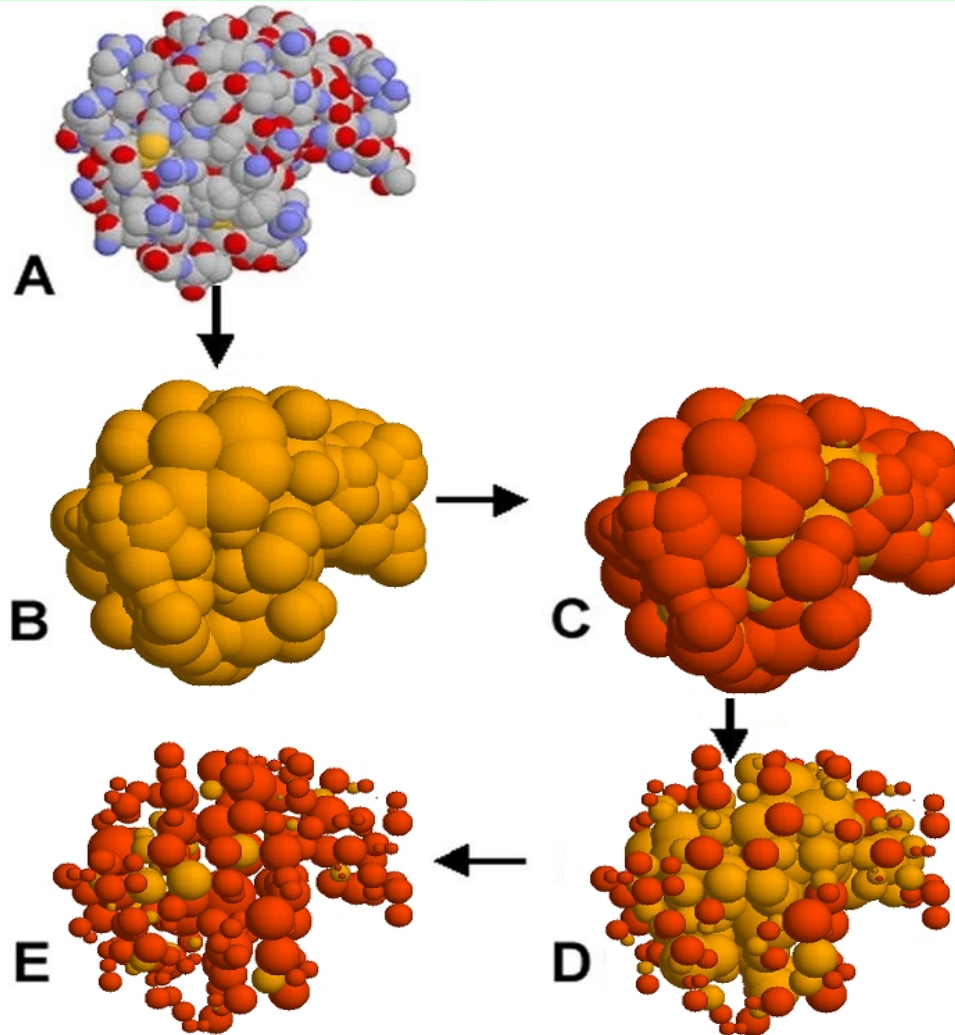
1 bead/cube in a variable-size cubic grid. Water of hydration, based on atom values, included in each bead.

A→B All the beads are generated and placed (CM or CC).

B→C Beads are screened for surface accessibility (ASA; red, accessible; orange, buried).

C→D Overlaps between the exposed beads are then removed, reducing the radii and outward translating the beads' centers.

D→E Overlaps between the buried beads are then removed, and they are re-screened for accessibility. Buried beads are excluded from hydrodynamic computations.



Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

Eur Biophys J

DOI 10.1007/s00249-009-0418-0

ORIGINAL PAPER

The implementation of SOMO (SOLUTION MOdeller) in the UltraScan analytical ultracentrifugation data analysis suite: enhanced capabilities allow the reliable hydrodynamic modeling of virtually any kind of biomacromolecule

Emre Brookes · Borries Demeler · Camillo Rosano ·
Mattia Rocco

mabi.200900474

Developments in the US-SOMO Bead Modeling Suite: New Features in the Direct Residue-to-Bead Method, Improved Grid Routines, and Influence of Accessible Surface Area Screening^a

Emre Brookes, Borries Demeler, Mattia Rocco*

Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

The screenshot displays the SOMO Solution Modeler software interface. The main window is titled "SOMO Solution Modeler" and contains several panels and a file information window.

Navigation and Main Panels:

- Lookup Tables SOMO MD PDB Configuration** (top menu)
- PDB Functions:**
 - Select Lookup Table: C:\Program Files\UltraScan\etc\somo.residue
 - Batch Mode/Cluster Operation
 - Load Single PDB File: rogram Files\Ultrascan\somo\demo\8RAT.pdb
 - Please select a PDB Structure: **Model: 1**
 - View/Edit PDB File | PDB Editor
 - SAXS/SANS Functions
 - Run DMD
 - BD
- Bead Model Functions:**
 - Bead Model Suffix: A20R50hiOT / A10R30syOThyG5 / A20R50
 - Overwrite existing filenames Add auto-generated suffix
 - Build SoMo Bead Model | Build AtoB (Grid) Bead Model
 - Build SoMo Overlap Bead Model | **Grid Existing Bead Model**
 - View ASA Results | **Visualize Bead Model**
 - Batch Mode/Cluster Operation | View Bead Model File
 - Load Single Bead Model File: not selected
 - SAXS/SANS Functions** | Automatically Calculate Hydrodynamics
- Hydrodynamic Calculations:**
 - Calculate RB Hydrodynamics SMI** | **Calculate RB Hydrodynamics ZENO**
 - Show Hydrodynamic Calculations** | Open Hydrodynamic Calculations File
 - Select Parameters to be Saved | Save parameters to file
 - BEST | Model classifier | **Stop** | Close
 - Help | Config

File Information Window (Right Panel):

File

All options set to default values
 PDB HEADER: HYDROLASE (NUCLEIC ACID,RNA) 13-AUG-91 8RAT
 PDB TITLE : EFFECTS OF TEMPERATURE ON PROTEIN STRUCTURE AND DYNAMICS: X-
 PDB TITLE : RAY CRYSTALLOGRAPHIC STUDIES OF THE PROTEIN RIBONUCLEASE-A
 PDB TITLE : AT NINE DIFFERENT TEMPERATURES FROM 98 TO 320 K

Residue sequence from 8RAT.pdb:
 LYS GLU THR ALA ALA ALA LYS PHE GLU ARG GLN HIS MET ASP SER SER THR SER ALA ALA SER SER SER ASN
 TYR CYS ASN GLN MET MET LYS SER ARG ASN LEU THR LYS ASP ARG CYS LYS PRO VAL ASN THR PHE VAL HIS
 GLU SER LEU ALA ASP VAL GLN ALA VAL CYS SER GLN LYS ASN VAL ALA CYS LYS ASN GLY GLN THR ASN CYS
 TYR GLN SER TYR SER THR MET SER ILE THR ASP CYS ARG GLU THR GLY SER SER LYS TYR PRO ASN CYS ALA
 TYR LYS THR THR GLN ALA ASN LYS HIS ILE ILE VAL ALA CYS GLU GLY ASN PRO TYR VAL PRO VAL HIS PHE ASP
 ALA SER VAL

Sequence in one letter code:
 KETAAAKFERQHMDSSSTSAASSSNYCNQMKSRNLTFRCKP
 VMTFVHESLADVQAVCSQRNVACKNGQTNCYQSYSTMSITDC
 RETGSSKYPNCAYKTTQANKHIIIVACEGNPYVPVHFDASV

Checking the pdb structure for model 1
 Loaded pdb file : ok

Model: 1 vbar 0.710 cm³/g

Model: 1 Chain: A Molecular weight 13683.9 Daltons, Volume (from vbar) 16122 A³, atomic volume 16514.2 A³ average electron density 0.441014 A⁻³

Model 1 Rg: 1.43 nm

Model: 1 Molecular weight 13683.9 Daltons, Volume (from vbar) 16122 A³, atomic volume 16514.2 A³ average electron density 0.441014 A⁻³
 8RAT model 1 13.68 kD, Rg 14.34 A, (Rg/6.5)³: 10.75 21.5 %

8RAT models selected: 1

Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

The screenshot displays the SOMO Solution Modeler software interface. The window title is "SOMO Solution Modeler". The interface is divided into several functional panels and a log window.

Lookup Tables SOMO MD PDB Configuration

PDB Functions:

- Select Lookup Table: C:\Program Files\UltraScan\etc\somo.residue
- Batch Mode/Cluster Operation
- Load Single PDB File: rogram Files\Ultrascan\somo\demo\8RAT.pdb
- Please select a PDB Structure: Model: 1
- View/Edit PDB File | PDB Editor
- SAXS/SANS Functions
- Run DMD
- BD

Bead Model Functions:

- Bead Model Suffix: A20R50hiOT-so
- Overwrite existing filenames Add auto-generated suffix
- Build SoMo Bead Model | Build AtoB (Grid) Bead Model
- Build SoMo Overlap Bead Model | Grid Existing Bead Model
- View ASA Results | Visualize Bead Model
- Batch Mode/Cluster Operation | View Bead Model File
- Load Single Bead Model File: 8RAT_1
- SAXS/SANS Functions Automatically Calculate Hydrodynamics

Hydrodynamic Calculations:

- Calculate RB Hydrodynamics SMI | Calculate RB Hydrodynamics ZENO
- Show Hydrodynamic Calculations | Open Hydrodynamic Calculations File
- Select Parameters to be Saved Save parameters to file
- BEST | Model classifier | Stop | Close
- Help | Config | 100%

File

```

1 will be included
ZENO calculation start
Calculate hydrodynamics (Zeno) completed
Visualizing model 1
Peptide Bond Rule is on for this PDB

All options set to default values

8RAT models selected: 1

Building the bead model for 8RAT model 1
Checking the pdb structure
PDB structure ok
There are 951 atoms in 2 chain(s) in this model
Creating beads from atomic model
Computing ASA via ASAB1
Return from Computing ASA
Anhydrous volume 16480.33 A^3
There are 246 beads in this model before popping
Begin popping stage 1
Beads popped 0.
Begin radial reduction stage 1
Begin popping stage 2
Beads popped 0.
Begin radial reduction stage 2
Begin popping stage 3
Beads popped 0.
Begin radial reduction stage 3
Finished with popping and radial reduction
Rechecking beads
0 previously buried beads are exposed by rechecking
Finished rechecking beads
Build bead model completed

All options set to default values

Begin hydrodynamic calculations

Model 1 will be included

Processing model 1 bead count 246 vbar 0.71
Using 98 beads for the matrix
Supermatrix inversion Cycle 1 of 3
Supermatrix inversion Cycle 2 of 3
Supermatrix inversion Cycle 3 of 3
Calculate hydrodynamics completed
    
```

Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

Add/Edit Hybridization

Add/Edit Atom

Add/Edit Residue

Add/Edit SAXS coefficients

SAXS/SANS Functions	
Run DMD	
BD	
Bead Model Functions:	
Bead Model Suffix:	A20R50hiOT-so
<input checked="" type="checkbox"/> Overwrite existing filenames	<input checked="" type="checkbox"/> Add auto-generated suffix
Build SoMo Bead Model	Build AtoB (Grid) Bead Model
Build SoMo Overlap Bead Model	Grid Existing Bead Model
View ASA Results	Visualize Bead Model
Batch Mode/Cluster Operation	View Bead Model File
Load Single Bead Model File	8RAT_1
SAXS/SANS Functions	<input type="checkbox"/> Automatically Calculate Hydrodynamics
Hydrodynamic Calculations:	
Calculate RB Hydrodynamics SMI	Calculate RB Hydrodynamics ZENO
Show Hydrodynamic Calculations	Open Hydrodynamic Calculations File
Select Parameters to be Saved	<input type="checkbox"/> Save parameters to file
BEST	Model classifier
Help	Config
<div style="text-align: center;"> Stop Close </div> <div style="text-align: center;"> 100% </div>	

The screenshot shows the US-SOMO software interface with a log window open. The log window displays the following text:

```

File 1 will be included
ZENO calculation start
Calculate hydrodynamics (Zeno) completed
Visualizing model 1
Peptide Bond Rule is on for this PDB

All options set to default values

8RAT models selected: 1

Building the bead model for 8RAT model 1
Checking the pdb structure
PDB structure ok
There are 951 atoms in 2 chain(s) in this model
Creating beads from atomic model
Computing ASA via ASAB1
Return from Computing ASA
Anhydrous volume 16480.33 A^3
There are 246 beads in this model before popping
Begin popping stage 1
Beads popped 0.
Begin radial reduction stage 1
Begin popping stage 2
Beads popped 0.
Begin radial reduction stage 2
Begin popping stage 3
Beads popped 0.
Begin radial reduction stage 3
Finished with popping and radial reduction
Rechecking beads
0 previously buried beads are exposed by rechecking
Finished rechecking beads
Build bead model completed

All options set to default values

Begin hydrodynamic calculations

Model 1 will be included

Processing model 1 bead count 246 vbar 0.71
Using 98 beads for the matrix
Supermatrix inversion Cycle 1 of 3
Supermatrix inversion Cycle 2 of 3
Supermatrix inversion Cycle 3 of 3
Calculate hydrodynamics completed
    
```


Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

The screenshot displays the 'SOMO Solution Modeler' application window. The main menu bar includes 'Lookup Tables', 'SOMO', 'MD', 'PDB', and 'Configuration'. A 'File' menu is open, showing '1 will be included'. The central dialog box is titled '1: Define Residue Properties:' and contains the following fields and controls:

- Load Atom Definition File:** /usr/local/ultrascan/etc/somo.atom
- Load Residue Definition File:** /usr/local/ultrascan/etc/somo.residue
- Residue Name:** TYR
- Description:** Tyrosine
- Number of Atoms In Residue:** 12 (with up/down arrows)
- Number of Beads for Residue:** 2 (with up/down arrows)
- Residue Type:** Amino Acid (with a dropdown arrow)
- Residue anhydrous mol. vol. (A³):** 197.00
- Residue partial spec. vol. (cm³/g):** 0.708
- Max. Accessible Surface Area (A²):** 228.00
- Number of Residues In File:** 74
- Accept Residue and Continue:** (button)

At the bottom of the dialog, a list of residue types is shown, with '13: Amino Acid, TYR (Tyrosine)' selected. The bottom status bar includes 'Help', 'Config', and a progress indicator at 100%.

Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

The screenshot displays the SOMO Solution Modeler software interface. The main window title is "SOMO Solution Modeler" and it includes a menu bar with "Lookup Tables", "SOMO", "MD", "PDB", "Configuration", and "File". The "File" menu is open, showing "1 will be included".

The primary dialog box is titled "2. Define Residue Atoms:" and contains the following fields and controls:

- Select Residue Atom to be defined:** Atom 1: N (N3H1, Positioning: no)
- Select Atom from Lookup Table:** N
- Select Hybridization for Atom:** N3H1
- Atom determines Position:** (Check if true)
- Hydration Number for Atom:** 1

At the bottom of the dialog are two buttons: "Assign Current Atom" and "Continue".

Below the dialog is a toolbar with various options:

- Build SoMo Bead Model
- Build AtoB (Grid) Bead Model
- Build SoMo Overlap Bead Model
- Grid Existing Bead Model
- View ASA Results
- Visualize Bead Model
- Batch Mode/Cluster Operation
- View Bead Model File
- Load Single Bead Model File
- 8RAT_1
- SAXS/SANS Functions
- Automatically Calculate Hydrodynamics

A section titled "Hydrodynamic Calculations:" contains:

- Calculate RB Hydrodynamics SMI
- Calculate RB Hydrodynamics ZENO
- Show Hydrodynamic Calculations
- Open Hydrodynamic Calculations File
- Select Parameters to be Saved
- Save parameters to file

At the bottom of the interface are buttons for "BEST", "Model classifier", "Stop", "Close", "Help", and "Config". A progress bar at the bottom right shows "100%".

The right-hand pane displays a log of operations:

```

Begin popping stage 3
Beads popped 0.
Begin radial reduction stage 3
Finished with popping and radial reduction
Rechecking beads
0 previously buried beads are exposed by rechecking
Finished rechecking beads
Build bead model completed

All options set to default values
Begin hydrodynamic calculations
Model 1 will be included

Processing model 1 bead count 246 vbar 0.71
Using 98 beads for the matrix
Supermatrix inversion Cycle 1 of 3
Supermatrix inversion Cycle 2 of 3
Supermatrix inversion Cycle 3 of 3
Calculate hydrodynamics completed
    
```

Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

SOMO Solution Modeler

Lookup Tables SOMO MD PDB Configuration File 1 will be included

3. Define Residue Bead Properties:

Select Residue Bead to be defined:	Bead 1: defined
Select Bead Color:	Blue (1)
Select Positioning Method:	Center of Gravity
This Bead Is part of the:	<input checked="" type="radio"/> Backbone <input type="radio"/> Sidechain
Currently defined Atoms for Bead:	Select Atom for Bead (multi-selection OK):
Atom 1: N (N3H1, Positioning: no) Atom 2: CA (C4H1, Positioning: no) Atom 3: C (C3H0, Positioning: yes) Atom 4: O (O1H0, Positioning: yes)	Atom 1: N (N3H1, Positioning: no) Atom 2: CA (C4H1, Positioning: no) Atom 3: C (C3H0, Positioning: yes) Atom 4: O (O1H0, Positioning: yes) Atom 5: CB (C4H2, Positioning: no) Atom 6: CG (C3H0, Positioning: no) Atom 7: CD1 (C3H1, Positioning: no) Atom 8: CD2 (C3H1, Positioning: no) Atom 9: CE1 (C3H1, Positioning: yes) Atom 10: CE2 (C3H1, Positioning: yes) Atom 11: CZ (C3H0, Positioning: no)
Bead Volume:	64.90
Bead Mol. Weight:	56.05
Bead Hydration from Atoms' Values:	1.000000
Override Bead Hydration Value:	1
Bead hydrated Volume, Radius:	88.94 A ³ , 2.77 A
Accept Bead Definition	Reset
Add Residue to File	Delete Residue
Help	Close

irt
 amics (Zeno) completed
 on for this PDB
 fault values
 ed: 1
 odel for 8RAT model 1
 ructure
 s in 2 chain(s) in this model
 atomic model
 ASAB1
 ting ASA
 16480.33 A³
 s in this model before popping
 : 1
 in stage 1
 : 2
 in stage 2
 : 3
 in stage 3
 g and radial reduction
 beads are exposed by rechecking
 beads
 mpleted
 fault values
 calculations
 led
 bead count 246 vbar 0.71
 the matrix
 in Cycle 1 of 3
 in Cycle 2 of 3
 in Cycle 3 of 3
 amics completed

Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

ASA Calculation

SoMo Overlap Reduction

AtoB (Grid) Overlap Reduction

Hydrodynamic Calculations

Miscellaneous Options

Bead Model Output

Grid Functions (AtoB)

SAXS Options

The screenshot displays the US-SOMO software interface. On the left is a menu with various options. The main window shows a log of operations:

```

File 1 will be included
ZENO calculation start
Calculate hydrodynamics (Zeno) completed
Visualizing model 1
Peptide Bond Rule is on for this PDB

All options set to default values

.pdb
8RAT models selected: 1

Building the bead model for 8RAT model 1
Checking the pdb structure
PDB structure ok
There are 951 atoms in 2 chain(s) in this model
Creating beads from atomic model
Computing ASA via ASAB1
Return from Computing ASA
Anhydrous volume 16480.33 A^3
There are 246 beads in this model before popping
Begin popping stage 1
Beads popped 0.
Begin radial reduction stage 1
Begin popping stage 2
Beads popped 0.
Begin radial reduction stage 2
Begin popping stage 3
Beads popped 0.
Begin radial reduction stage 3
Finished with popping and radial reduction
Rechecking beads
0 previously buried beads are exposed by rechecking
Finished rechecking beads
Build bead model completed

All options set to default values

Begin hydrodynamic calculations

Model 1 will be included

Processing model 1 bead count 246 vbar 0.71
Using 98 beads for the matrix
Supermatrix inversion Cycle 1 of 3
Supermatrix inversion Cycle 2 of 3
Supermatrix inversion Cycle 3 of 3
Calculate hydrodynamics completed
    
```

The interface includes a menu with the following items:

- Build SoMo Bead Model
- Build AtoB (Grid) Bead Model
- Build SoMo Overlap Bead Model
- Grid Existing Bead Model
- View ASA Results
- Visualize Bead Model
- Batch Mode/Cluster Operation
- View Bead Model File
- Load Single Bead Model File
- 8RAT_1
- SAXS/SANS Functions
- Automatically Calculate Hydrodynamics
- Hydrodynamic Calculations:**
- Calculate RB Hydrodynamics SMI
- Calculate RB Hydrodynamics ZENO
- Show Hydrodynamic Calculations
- Open Hydrodynamic Calculations File
- Select Parameters to be Saved
- Save parameters to file
- BEST
- Model classifier
- Stop
- Close
- Help
- Config

A progress bar at the bottom indicates 100% completion.

Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

The image shows a screenshot of the SOMO Solution Modeler software interface. The main window is titled "SOMO Solution Modeler" and has a menu bar with "Lookup Tables", "SOMO", "MD", "PDB", "Configuration", and "File". A dialog box titled "SOMO Accessible Surface Area Options" is open in the foreground. The dialog box has a title bar with a red background and the text "SOMO Accessible Surface Area Options". Inside the dialog box, there is a section titled "Accessible Surface Area Options:" with two checked checkboxes: "Perform ASA Calculation" and "Re-check bead ASA". Below this, there is a section for "ASA Method:" with two options: "Voronoi Tessellation (Surface, Tsodikov et al.)" (unchecked) and "Rolling Sphere (ASAB1, Lee & Richards' Method)" (checked). The dialog box also contains several input fields with spinners and up/down arrows, each with a label and a value: "ASA Probe Radius (A):" (1.4), "ASA Probe Recheck Radius (A):" (1.4), "SOMO ASA Threshold (A^2):" (20), "SOMO Bead ASA Threshold %:" (50), "Grid ASA Threshold (A^2):" (10), "Grid Bead ASA Threshold %:" (30), and "ASAB1 Step Size (A):" (1). At the bottom of the dialog box are two buttons: "Help" and "Close". In the background, a log window is visible with the following text: "start", "dynamics (Zeno) completed", "1", "is on for this PDB", "default values", "ected: 1", "model for 8RAT model 1", "structure", "oms in 2 chain(s) in this model", "rom atomic model", "ia ASAB1", "puting ASA", "e 16480.33 A^3", "ads in this model before popping", "age 1", "ction stage 1", "age 2", "ction stage 2", "age 3", "ction stage 3", "pping and radial reduction", "S", "ed beads are exposed by rechecking", "ng beads", "completed", "default values", "mic calculations", "cluded", "1 bead count 246 vbar 0.71", "or the matrix", "rsion Cycle 1 of 3", "rsion Cycle 2 of 3", "rsion Cycle 3 of 3", "dynamics completed". At the bottom of the main window, there is a status bar with "Help", "Config", and a progress indicator showing "100%".

Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

The screenshot displays the SOMO Solution Modeler software interface. The main window has a menu bar with 'Lookup Tables', 'SOMO', 'MD', 'PDB', 'Configuration', and 'File'. A sub-window titled 'SoMo Bead Overlap Reduction Options' is open, showing the following settings:

- SoMo Bead Overlap Reduction Options:**
- Bead Overlap Tolerance:** 0.001
- Exposed Side chain beads | Exposed Main and side chain beads | Buried beads
- Overlap reduction between exposed side chain beads**
- Fuse Beads that overlap by more than: 70
- Remove Overlaps
- Overlap Reduction Step Size (In %):**
- Remove Overlaps synchronously: 1
- Remove Overlaps hierarchically (larger -> smaller) 1
- Outward Translation
- Buttons: Help, Close

At the bottom of the interface, there is a task bar with the following buttons: Calculate RB Hydrodynamics SMI, Calculate RB Hydrodynamics ZENO, Show Hydrodynamic Calculations, Open Hydrodynamic Calculations File, Select Parameters to be Saved, Save parameters to file (unchecked), BEST, Model classifier, Stop, Close, Help, Config, and a progress bar showing 100%.

On the right side of the main window, a status area displays the following text:

```
Processing model 1 bead count 246 vbar 0.71
Using 98 beads for the matrix
Supermatrix inversion Cycle 1 of 3
Supermatrix inversion Cycle 2 of 3
Supermatrix inversion Cycle 3 of 3
Calculate hydrodynamics completed
```

Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

The screenshot displays the SOMO Solution Modeler software interface. The main window title is "SOMO Solution Modeler". The menu bar includes "Lookup Tables", "SOMO", "MD", "PDB", "Configuration", and "File". A dialog box titled "Grid Bead Overlap Reduction Options" is open, showing the following settings:

- Grid Bead Overlap Reduction Options:**
 - Bead Overlap Tolerance:** 0.001
 - Exposed grid beads | Buried grid beads | Non-screened grid beads
 - Overlap reduction between exposed grid beads:**
 - Fuse Beads that overlap by more than: 0
 - Remove Overlaps
 - Remove Overlaps synchronously: 1
 - Remove Overlaps hierarchically (larger -> smaller): 1
 - Outward Translation
 - Overlap Reduction Step Size (In %):** 1

Buttons: Help, Close

Bottom panel:

- Calculate RB Hydrodynamics SMI | Calculate RB Hydrodynamics ZENO
- Show Hydrodynamic Calculations | Open Hydrodynamic Calculations File
- Select Parameters to be Saved | Save parameters to file
- BEST | Model classifier | Stop | Close
- Help | Config | 100%

Processing model 1 bead count 246 vbar 0.71
Using 98 beads for the matrix
Supermatrix inversion Cycle 1 of 3
Supermatrix inversion Cycle 2 of 3
Supermatrix inversion Cycle 3 of 3
Calculate hydrodynamics completed

Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

The screenshot displays the SOMO Solution Modeler software interface. The main window title is "SOMO Solution Modeler" and it includes a menu bar with "Lookup Tables", "SOMO", "MD", "PDB", "Configuration", and "File". A sub-window titled "SOMO Grid Function Options (AtoB)" is open, showing the following settings:

- Computations Relative to:**
 - Center of Mass
 - Center of Cubelet
- Cube Side (Angstrom):** 5
- Apply Cubic Grid
- Add theoretical hydration (PDB only)
- Expand Beads to Tangency
- Enable ASA screening

Buttons for "Adjust Overlap Options", "Help", and "Close" are visible in the dialog. The main application window shows a progress bar at 100% and a status area with the following text:

```

Finished with popping and radial reduction
Rechecking beads
0 previously buried beads are exposed by rechecking
Finished rechecking beads
Build bead model completed

All options set to default values
Begin hydrodynamic calculations
Model 1 will be included

Processing model 1 bead count 246 vbar 0.71
Using 98 beads for the matrix
Supermatrix inversion Cycle 1 of 3
Supermatrix inversion Cycle 2 of 3
Supermatrix inversion Cycle 3 of 3
Calculate hydrodynamics completed
    
```

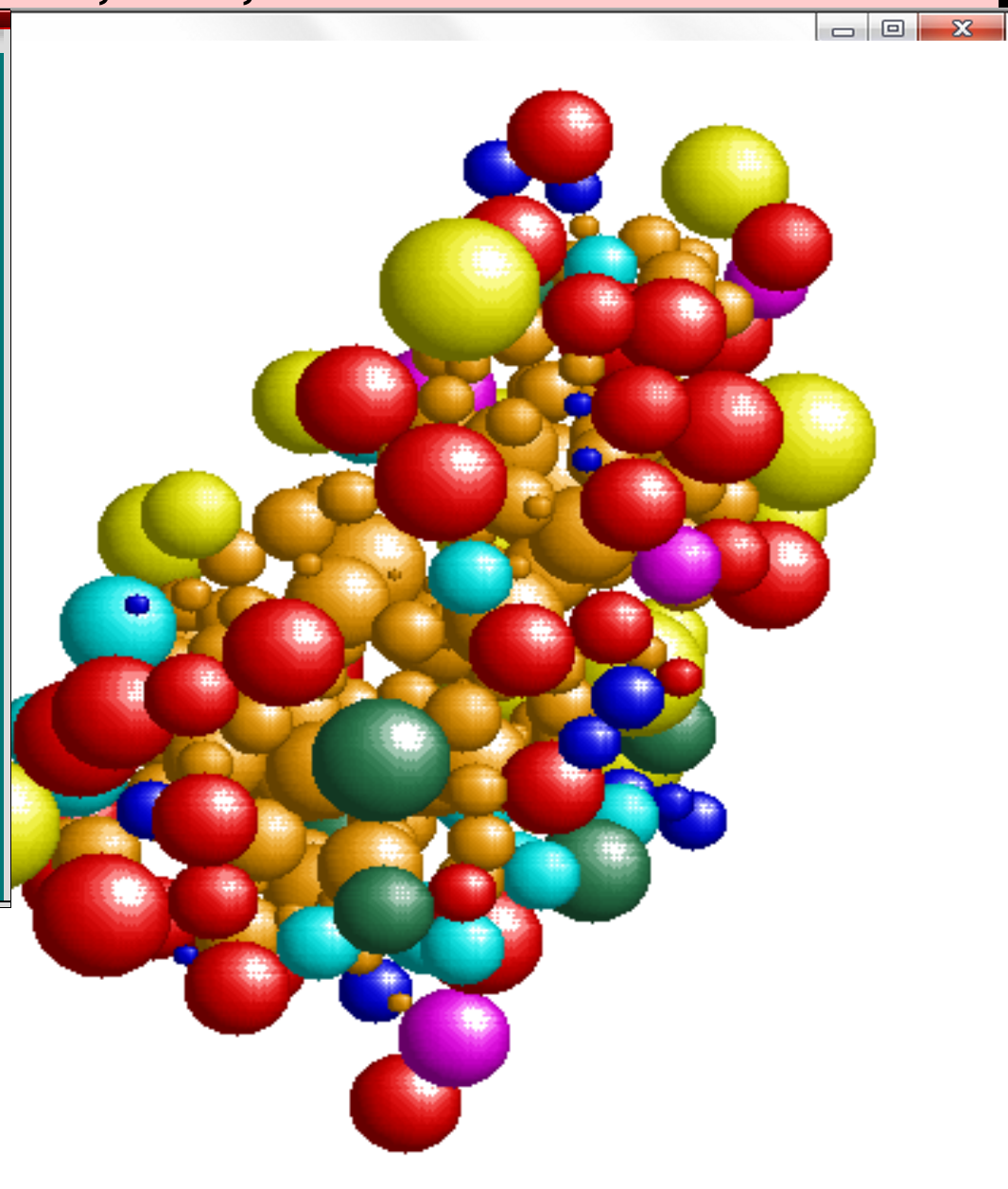
The bottom of the interface features a control panel with buttons for "View ASA Results", "Visualize Bead Model", "Batch Mode/Cluster Operation", "View Bead Model File", "Load Single Bead Model File" (with "8RAT_1" selected), "SAXS/SANS Functions", "Automatically Calculate Hydrodynamics", "Hydrodynamic Calculations:" section with "Calculate RB Hydrodynamics SMI", "Calculate RB Hydrodynamics ZENO", "Show Hydrodynamic Calculations", "Open Hydrodynamic Calculations File", "Select Parameters to be Saved", "Save parameters to file", "BEST", "Model classifier", "Stop", "Close", "Help", and "Config".

Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

SOMO Hydrodynamic Results

SOMO Hydrodynamic Results (Water at 20°C):

Total Beads in Model:	246
Used Beads in Model:	98
Molecular Mass:	1.3681e+04 Da
Part. Specif. Volume:	0.710 cm ³ /g
s(20,w):	1.93e+00 S
D(20,w), transl.:	1.18e-06 cm/sec ²
Stokes Radius:	1.81e+00 nm
Radius of Gyration:	1.48e+00 nm
Relaxation Time, tau(h):	7.81e+00 ns
Intrinsic Viscosity:	3.24e+00 cm ³ /g



Hydrodynamic Calculations:

<input type="button" value="Calculate RB Hydrodynamics SMI"/>	<input type="button" value="Calculate RB Hydrodynamics SMI"/>
<input type="button" value="Show Hydrodynamic Calculations"/>	<input type="button" value="Open Hydrodynamic Calculations"/>
<input type="button" value="Select Parameters to be Saved"/>	<input type="checkbox"/> Save parameters to file
<input type="button" value="BEST"/>	<input type="button" value="Model classifier"/>
<input type="button" value="Help"/>	<input type="button" value="Config"/>

100%

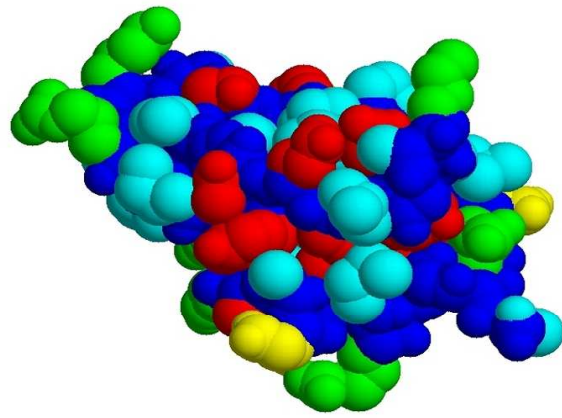
Layout and features of US-SOMO, integrated in UltraScan and available for Linux, Win, and Mac

The image displays the SOMO Solution Modeler software interface, which is integrated into UltraScan. The interface is divided into several functional panels:

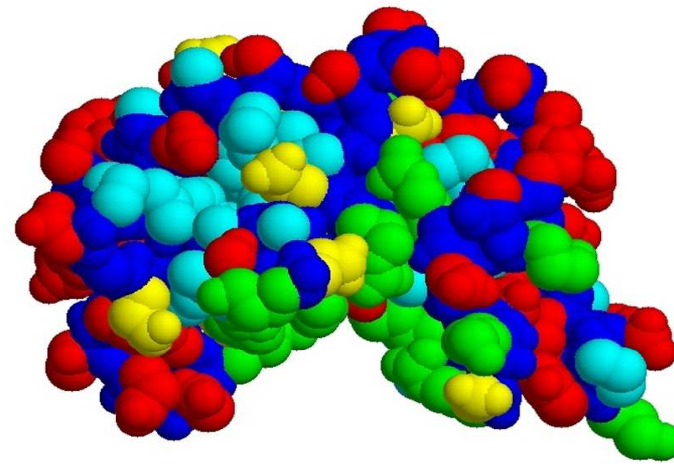
- PDB Functions:** Includes buttons for "Select Lookup Table" (pointing to C:\Program Files\UltraScan), "Batch Mode/Cluster Operation", "Load Single PDB File" (pointing to Program Files\Ultrascan\so), "Please select a PDB Structure:" (set to Model: 1), "View/Edit PDB File" (with a sub-button for "PDB Editor"), "SAXS/SANS Functions", "Run DMD", and "BD".
- Bead Model Functions:** Includes "Bead Model Suffix:" (A20R50hiC), checkboxes for "Overwrite existing filenames" and "Add auto-generated su", "Build SoMo Bead Model" (with sub-button "Build AtoB (Grid)"), "Build SoMo Overlap Bead Model" (with sub-button "Grid Existing Be"), "View ASA Results" (with sub-button "Visualize Bead"), "Batch Mode/Cluster Operation" (with sub-button "View Bead Mo"), "Load Single Bead Model File" (pointing to 8RAT_), "SAXS/SANS Functions" (with checkbox "Automatically Calculat"), "Calculate RB Hydrodynamics SMI" (with sub-button "Calculate RB Hydrod"), "Show Hydrodynamic Calculations" (with sub-button "Open Hydrodynamic C"), "Select Parameters to be Saved" (with checkbox "Save parameters to file"), "BEST" (with sub-button "Model classifier"), "Help" (with sub-button "Config"), and a "Stop" button.

At the bottom right of the interface, a green progress bar indicates 100% completion. To the right of the software window, a 3D molecular model is shown, consisting of numerous colored spheres (red, yellow, orange, blue, green, purple) representing atoms or beads in a complex, branched structure.

PDB

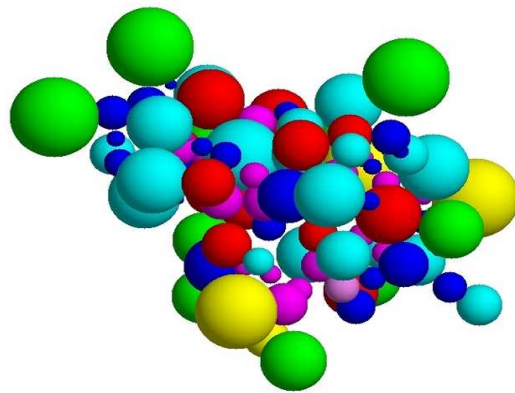


4PTI

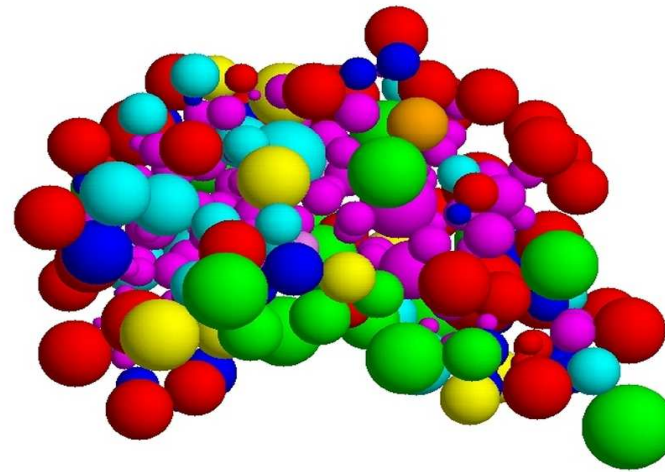


1XPS

SOMO



BPTI



RNase A

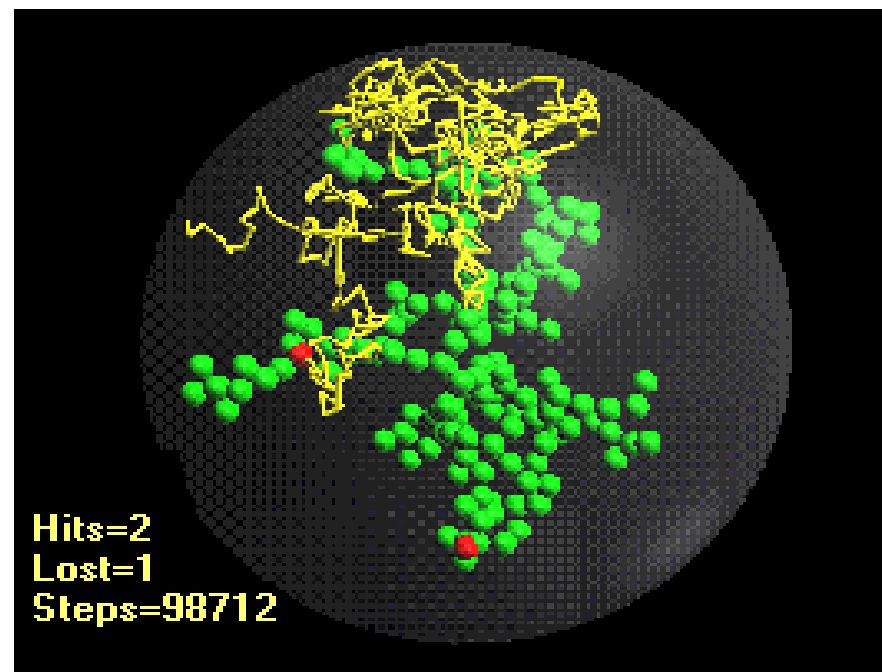
Other hydrodynamic computations methods

ZENO – Developed by Mansfield, Kang and Douglas (Stevens Institute and NIST)

BEST – Developed by S. Aragon, SFSU, CA

Scientific Principle of Program:

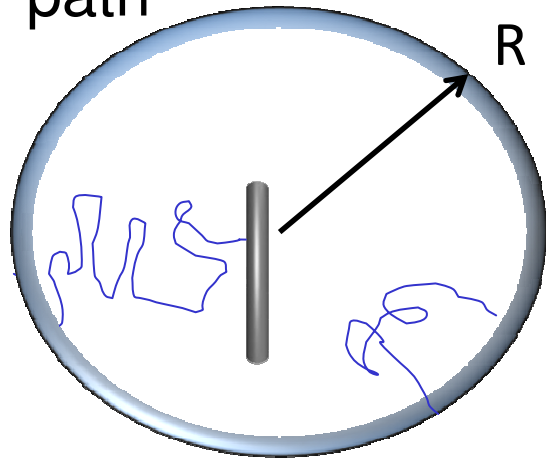
The Zeno computational method involves enclosing an arbitrary-shaped probed object within a sphere and launching random walks from this sphere. The probing trajectories either hit or return to the launch surface ('loss') as shown in the figure for a model soot particle aggregate, whereupon the trajectory is either terminated or reinitiated.



The fraction of random walk trajectories that hit the probed object determines its capacity C (hydrodynamic radius) and the electric polarizability tensor α and $[\eta]$ are estimated similarly.

ZENO: A Monte Carlo Numerical Path Integrator

Hitting path



Escaping path

$$\beta = \frac{\# hits}{\# attempts}$$

$$R_H = \beta R$$

$$fr = 6\pi\eta R_H$$

$$D = \frac{kT}{6\pi\eta R_H}$$

ZENO computes:

- electric Polarizability Tensor,
 - self-capacity,
 - intrinsic conductivity
 - Intrinsic viscosity
 - hydrodynamic radius
 - translational diffusion coefficient
 - translational friction coefficient
 - radius of gyration
 - structure factor...
- of **arbitrarily shaped objects**

Douglas & Zhou & Hubbard, *PRE*, Vol 49, Page 5319, (1994).

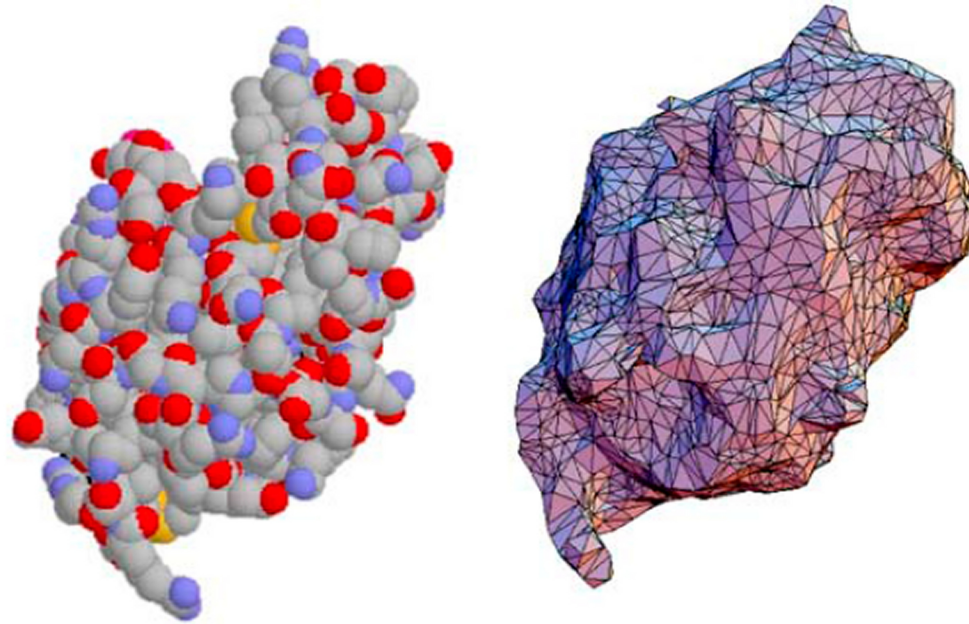
Douglas & Garboczi, *Adv. Chem. Phys*, Vol 91, Pages 85-153,(1995).

Mansfield et al., *PRE*, Vol 53, Vol 64, Pages 061401-16, 2001

Mansfield & Douglas, *PRE*, Vol 81, 021803 (2010)

<http://web.stevens.edu/zeno/>

BEST principles



BEST uses a very precise boundary element numerical solution of the exact formulation of the hydrodynamic resistance problem with stick boundary conditions to compute the full transport tensors in the center of resistance or the center of diffusion for an arbitrarily shaped rigid body, including rotation-translation coupling.

The input for BEST is a triangulation of the solvent-defined surface of the molecule of interest, given by Connolly's MSROLL. The triangulation is prepared for BEST by COALESCE, a program that allows user control over the quality and number of triangles to describe the surface. The computations are repeated for a series of triangulated structures with different number of plates, and extrapolated to zero plate size.

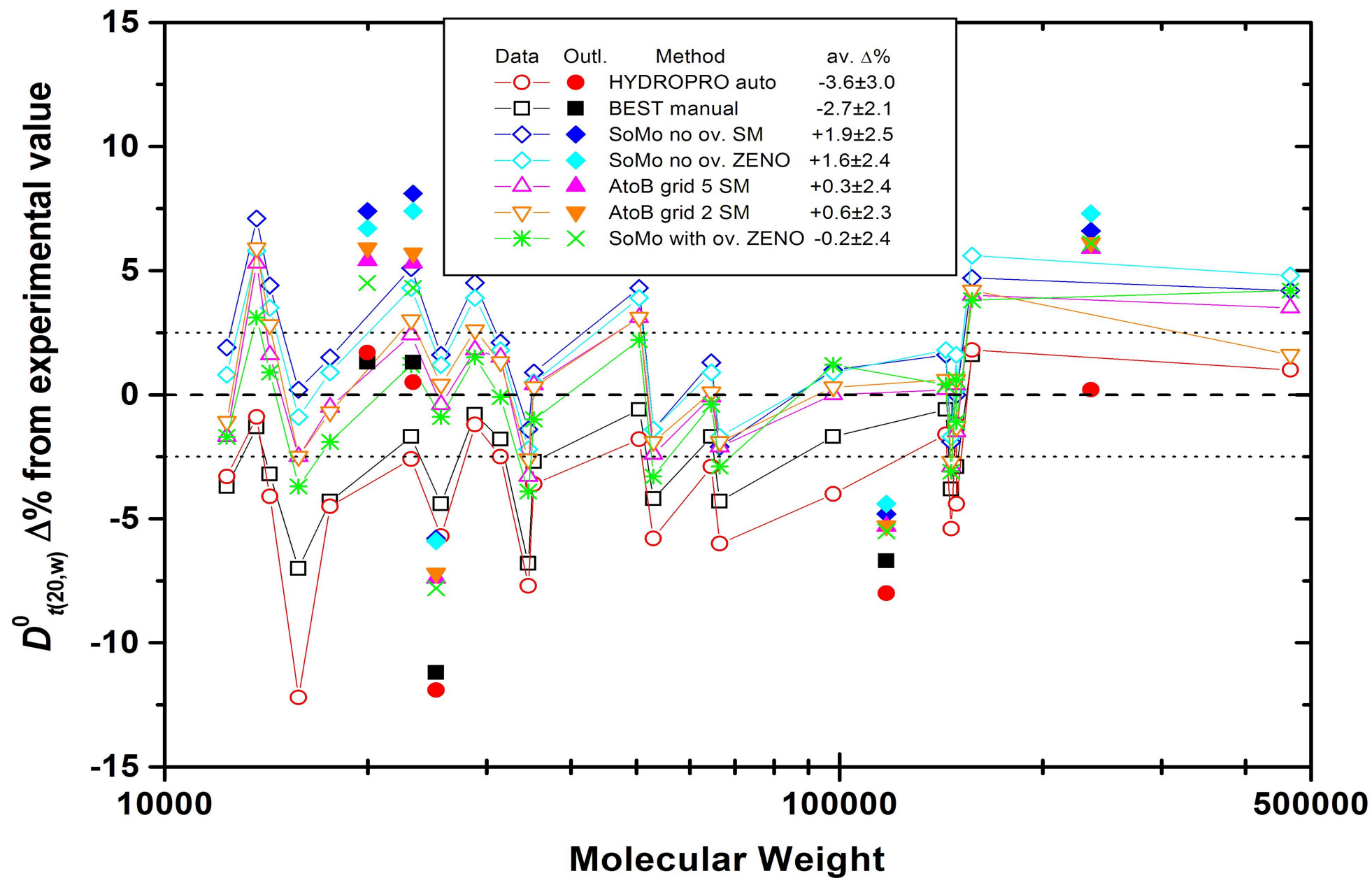
How to reliably test the methods?

- We chose to investigate in depth only the translational friction data, namely $D_{t(20,w)}^0$ and $s_{(20,w)}^0$.
- We have collected literature data, and carefully analyzed them for proper extrapolation and reduction to standard conditions.
- We selected PDB crystal structures from the same species as the experimental data.
- We performed the computations on those structures using SoMo, SoMo+Zeno, AtoB with two different grid sizes, BEST (all using the US-SOMO interface), and HYDROPRO (externally).

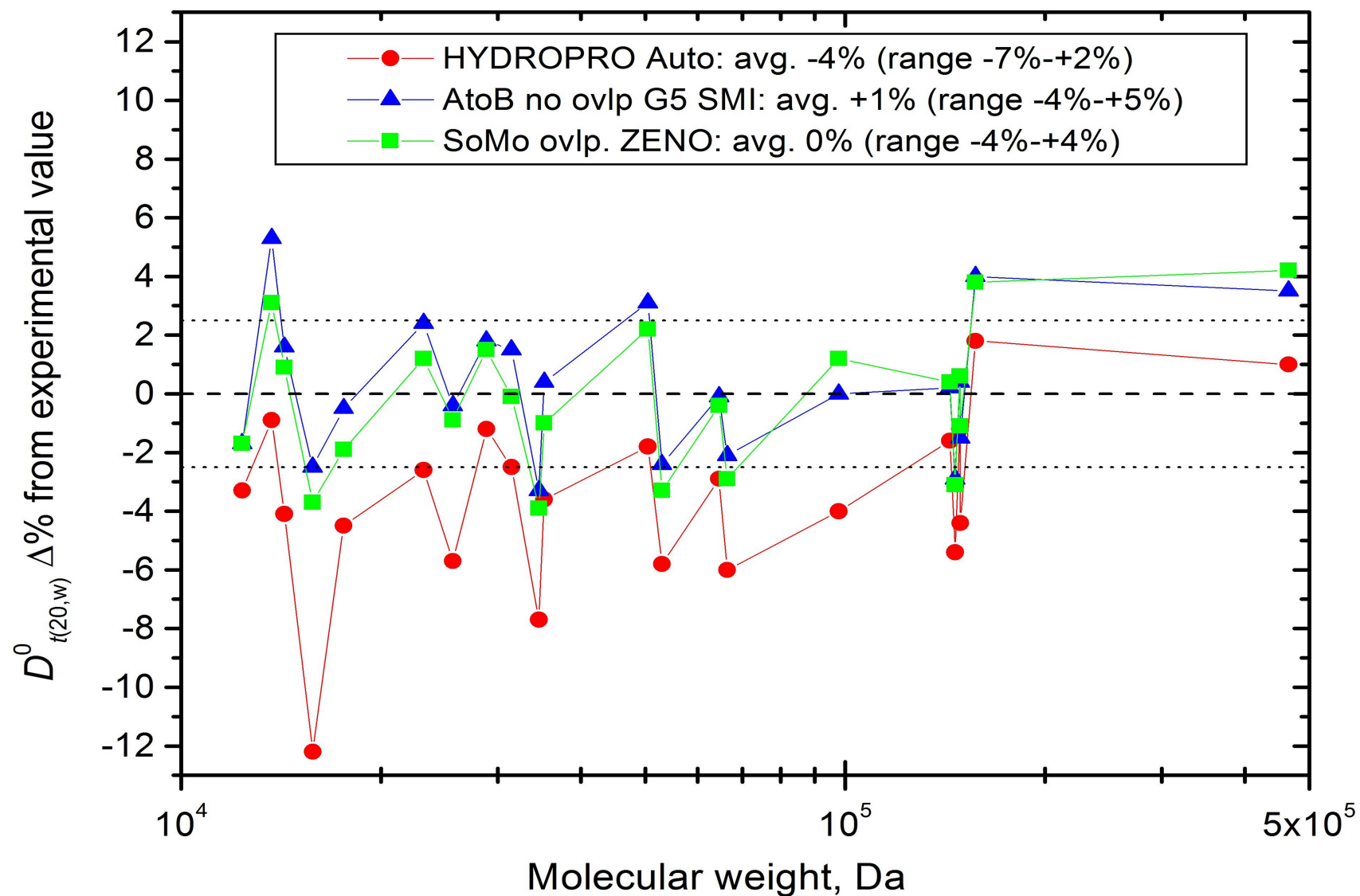
Test proteins used

#	Monomeric proteins	MW	#	Multimeric proteins	MW
1	Cytochrome c (1HRC)	12357.5	14	Superoxide dismutase (2SOD)	31442.2
2	Ribonuclease A (8RAT)	13683.8	15	β -Lactoglobulin (1BEB)	35224.7
3	α -Lactalbumin (1A4V+carb)	15784.7	16	α -Chymotrypsin (4CHA)	50473.5
4	Lysozyme (1AKI)	14306.7	17	Triosephosph. Isom. (1YPI)	52971.4
5	Myoglobin horse CO (1DWR)	17568.3	18	Hemoglobin CO (1HCO)	64559.7
6	Soybean Trypsin Inh. (1AVU)	19962.8	19	Citrate Synthase (1CTS)	97845.5
7	β -Trypsin (1TPO)	23335.9	20	Inorganic Pyrophosph. (1FAJ)	117339.0
8	Trypsinogen (1TGN)	23182.7	21	G3PD apo (2GD1)	143787.8
9	α -Chymotrypsin (4CHA)	25236.5	22	G3PD holo (1GD1)	146437.7
10	Chymotrypsinogen A (2CGA)	25659.0	23	LDH pig H + NAD (5LDH)	148942.6
11	Carbonic Anhydr. B (2CAB)	28820.5	24	LDH pig M + NAD (9LDH)	149063.5
12	Pepsin (4PEP)	34588.6	25	Aldolase (1ADO)	157136.0
13	H. Serum Albumin (1AO6)	66428.6	26	Catalase (4BLC)	235782.0
			27	β -Galactosidase (1BGL)	465557.0

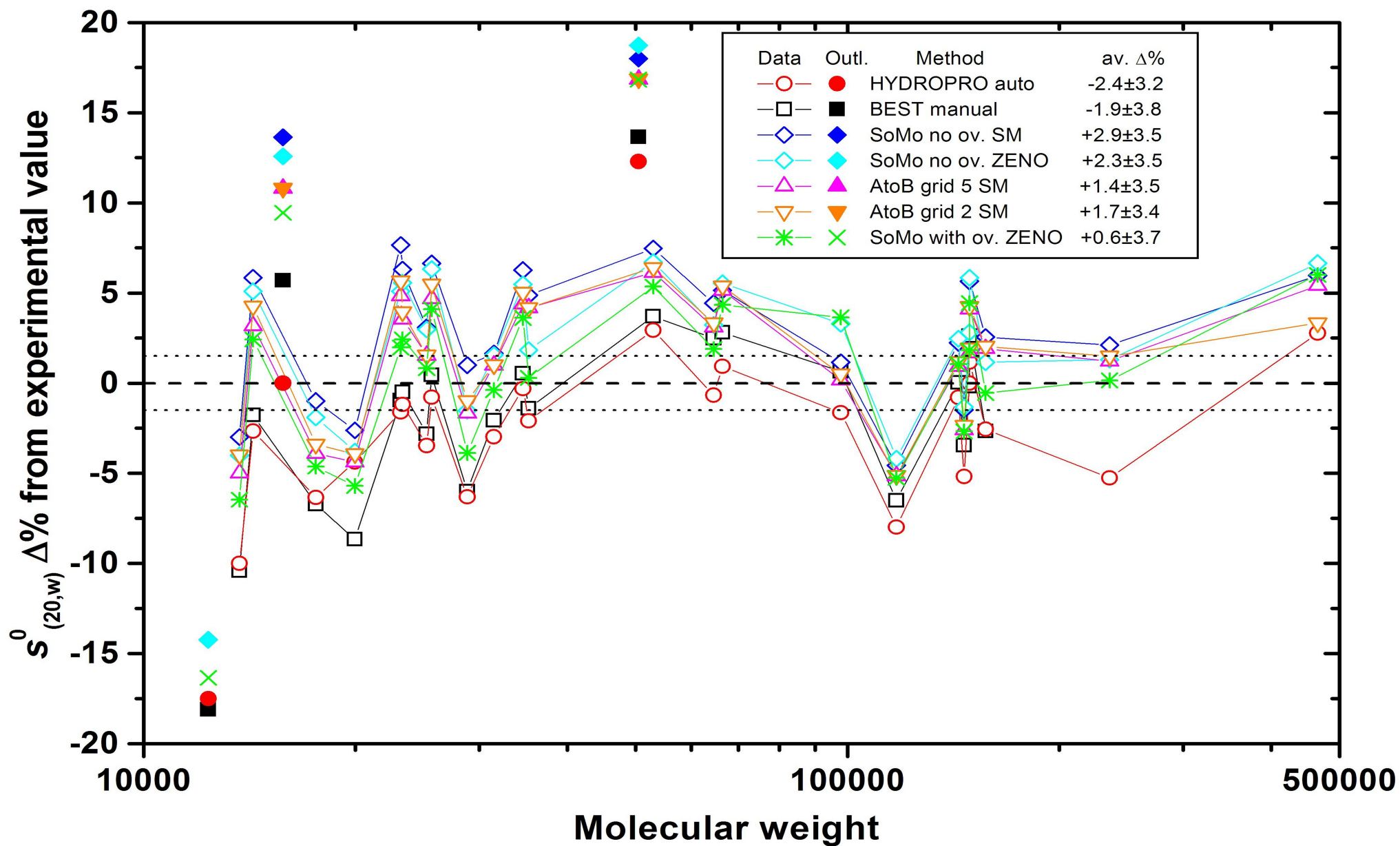
Overall performance of the different hydrodynamic modeling methods: D_t



Comparison between hydrodynamic calculations methods using 21 test proteins: translational diffusion coefficient



Overall performance of the different hydrodynamic modeling methods: *s*



Comparison conclusions:

- D_t is always better matched than s . This is likely due to poor psv knowledge/estimation.
- HYDROPRO and BEST both underestimate D_t and s . This is likely due to an excessive expansion of the surface in an attempt to account for hydration.
- SoMo with overlap removal overestimates D_t and s . This is likely due to an excessive shrinkage of the hydrated beads notwithstanding the outward translation.
- AtoB with a 5 Å grid appears to produce reasonable hydrated surfaces leading to very good D_t matching.
- The combination of SoMo models without overlap removal and Zeno computations produces the best D_t matching.